

**Happiness and the heart:  
an investigation into the mechanisms linking psychological  
well-being, work stress and cardiovascular disease**

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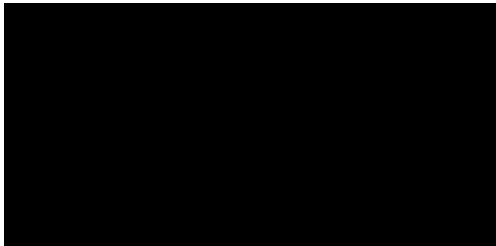
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I, Sophie Bostock, confirm that the work presented in this thesis is my own.

Where information has been derived from other sources, I confirm that this has been indicated in the thesis.



'He made her melancholy, sad, and heavy;  
And so she died: had she been light, like you,  
Of such a merry, nimble, stirring spirit,  
She might ha' been a grandam ere she died:  
And so may you; *for a light heart lives long.*'

Love's Labour's Lost (Act V, Scene II)

William Shakespeare, first published 1598

## **Abstract**

Prospective studies have reported that positive psychological well-being is associated with a reduced risk of cardiovascular disease. Direct psychobiological processes have been implicated in this association. It is unclear to what extent well-being predicts health outcomes independently of chronic stressors, such as job strain. This thesis explores associations between well-being, job strain and outcomes relevant to cardiovascular disease in four empirical studies. Two biomarkers are investigated: cortisol, a neuroendocrine marker, and blood pressure.

In study one, higher positive emotions over one week predicted lower reported stress during a standardised laboratory mental stress task, lower cortisol responses and faster blood pressure recovery. In study two, cross-sectional analyses of employee surveys indicated that low positive affect could mediate associations between job strain and fatigue, but reverse associations could not be discounted. Study three showed that job strain predicted heightened evening cortisol and a flatter diurnal rhythm in shift workers. Positive affect was not associated with cortisol. The hypothesis emerged that intervening to increase well-being might reduce perceived job strain and associated physiological activation. Study four tested this hypothesis in healthy workers using a mindfulness meditation smartphone application to promote well-being. The intervention was associated with increased well-being, reduced job strain and a trend for lower blood pressure after eight weeks. Decreased negative affect, not positive affect, predicted blood pressure declines. Changes in hair cortisol concentration were not associated with the intervention or psychological outcomes.

Well-being appears to predict favourable cognitive appraisals of the work environment. Frequent positive emotions may reduce autonomic activation directly or via a reduction in negative emotion. Intervention findings suggested that self-guided mindfulness meditation practice enhanced well-being in the short term but effects on blood pressure and cortisol were inconclusive. Further research to examine longer term effects on psychological and biological outcomes is warranted to determine whether mindfulness-based therapies could play a role in cardiovascular disease prevention.



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## Introduction

Improving well-being has become an increasingly high profile goal for national and international policy in recent years. Traditional economic indicators of performance, such as Gross Domestic Product, have been criticised as incomplete and unsustainable as indicators of societal progress (Jackson, 2009; Michaelson et al., 2009). Gains in economic growth have not been reflected in individuals' assessments of quality of life (Hall et al., 2010). The Commission on the Measurement of Economic Performance and Social Progress, commissioned by President Sarkozy, concluded that subjective measures of well-being could be both "*meaningful and reliable*" and called for a "*shift [of] emphasis from measuring economic production to measuring people's well-being*" (Stiglitz et al., 2009).

This political shift has led to increased scrutiny of how well-being is defined and measured (Eurostat, 2011; OECD, 2011). In the UK, a national programme to measure well-being was launched in November 2010, led by the Office of National Statistics. In April 2012, the United Nations convened its first conference on happiness. On 20 March 2013, the first International Day of Happiness was proclaimed by the UN General Assembly to promote happiness as a universal goal. The UN acknowledged that to attain global happiness, economic development must be accompanied by social and environmental well-being.<sup>1</sup>

In an overview of the research into factors influencing well-being, the UN conference report referred to a two-way interaction between health and happiness, stating that while physical health may improve happiness, "*happiness improves physical health*."<sup>2</sup> The assumption that happiness improves health is not new, for example, the Bible book of Proverbs states "*A merry heart doeth good like a medicine: but a broken spirit drieth the bones*" (Proverbs 17:22, KJV).<sup>3</sup> Shakespeare wrote in *Love's Labour's Lost* in the late sixteenth century "*a light heart lives long*" (Act V, Scene II). Despite this established perception of an association between happiness and health, the scientific study of psychological well-being (as opposed to mental ill health) and its links with biology and

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<sup>1</sup> <http://www.un.org/en/events/happinessday/index.shtml>, accessed August 2013

<sup>2</sup> UN World Happiness Report, Helliwell et al. (2012), p9.

<sup>3</sup> quotation from King James Bible, authorised version, Cambridge Edition



health outcomes has emerged largely within the last twenty years. 'Positive psychology' was coined in 2000 as a term for the scientific study of optimal human functioning (Seligman and Csikszentmihalyi, 2000). Mainstream news coverage of prospective epidemiological research on this topic strongly suggests a protective effect of well-being against heart disease. For example, an article for *The Guardian* in February 2010 was headed "*Happiness reduces risk of heart disease, research finds; Boosting good feelings could help prevent condition*". In April 2012, the BBC online health pages led with the heading "*Being an optimist may protect against heart problems*".<sup>4</sup>

If these news headlines and the extract from the UN conference report can be believed, 'boosting good feelings' could be used as a novel public health strategy. Heart disease and related cardiovascular diseases are the most common cause of death in the UK and globally so effective strategies to prevent disease or slow its progression have huge potential benefits (Townsend et al., 2012). However, if well-being is not protective against heart disease, advice based on this assumption would be ineffective at best, and at worst, could reinforce a perspective which risks blaming the victim (Coyne and Tennen, 2010).

The over-arching aim of this thesis is to improve current understanding of the relationship between subjective well-being and the mechanisms leading to cardiovascular disease. In order to determine whether a factor has a causal association with disease epidemiologists often refer to the nine criteria identified by Bradford Hill in 1965. These are strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment and analogy (Hill, 1965). In Chapter 1, I explain how well-being can be defined and measured. I review evidence from prospective epidemiological studies which have reported on the temporal relationship between baseline well-being and cardiovascular disease incidence or progression. This permits some consideration of the strength, consistency and gradient of association, though comparability between studies is hampered by different measures of well-being.

In Chapter 2, I outline the evidence for plausible mechanisms linking well-being to cardiovascular disease processes. Behavioural, genetic and psychobiological pathways

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<sup>4</sup> <http://www.guardian.co.uk/society/2010/feb/18/happiness-reduces-heart-disease-risk>, <http://www.bbc.co.uk/news/health-17733371>, pages accessed August 2013

have been implicated. I focus on evaluating the evidence which relates well-being to dysregulation of the autonomic nervous system and neuroendocrine system. Chapter 3 describes an empirical investigation to expand the evidence by testing whether young women's experiences of positive emotions over a week predicted subjective, blood pressure or cortisol responses to an acute stress task under controlled conditions.

Bradford Hill's criterion 'specificity' can refer both to the relationship between a cause and a specific disease and the likelihood of there being no other likely explanation. In terms of a causal association between well-being and heart disease, the difficulty of confirming specificity is that low psychological well-being is typically associated with high levels of psychological distress. Psychosocial distress, which includes disorders such as anxiety and depression, hostile personality traits and chronic environmental stress, is an established risk factor for cardiovascular disease (NICE, 2010). A critical question for this thesis is whether well-being and positive states are equivalent to the absence of negative states or psychological distress, or whether positive well-being has independent protective effects against cardiovascular disease. Although epidemiological studies typically adjust for depressive symptoms, the relationship between well-being and chronic stressors is rarely discussed.

Chapter 4 introduces job strain, a chronic environmental stressor which, like well-being, has been linked to autonomic and neuroendocrine regulation and cardiovascular risk. Chapters 4, 5 and 6 consider alternative relationships between well-being and job strain in the aetiology of disease. Chapter 5 uses data from a cross-sectional employee survey to investigate whether well-being could mediate associations between job strain and fatigue, or whether independent pathways are more plausible. Chapter 6 describes a monitoring study which tested associations between job strain and positive affect with the diurnal cortisol rhythm during work and rest days.

Experiment, according to Hill's criteria, can reveal the strongest support for a causal hypothesis. Is it possible to deliberately enhance well-being to drive improvements in cardiovascular health? Psychosocial interventions to relieve depression in heart disease patients have demonstrated little influence on cardiac outcomes (Whalley et al. 2011). If well-being has independent protective effects on cardiovascular disease processes, an intervention which promotes positive psychological functioning could have benefits over

and above the relief of depression. Chapter 7 discusses the evidence for interventions which have explicitly targeted positive emotions, as opposed to relieving psychological distress. I identify mindfulness meditation as a therapeutic approach which may predominantly increase positive emotions. Chapter 8 describes a workplace trial which I implemented to test the hypothesis that increasing well-being using a mindfulness meditation smartphone application would reduce job strain, blood pressure and cortisol, without altering the work environment. Chapter 9, the final discussion, summarises the key findings and the overall contribution of this thesis to the literature.

## **Chapter 1 Positive psychological well-being and the risk of cardiovascular disease**

In this chapter I review the evidence linking subjective well-being to cardiovascular outcomes. Section 1.1 outlines why the prevention of cardiovascular disease is a public health priority and describes conventional risk factors, focussing on the risks attributed to psychosocial factors. Section 1.2 discusses how to define and measure subjective well-being. Section 1.3 discusses some of the key determinants of well-being, including relationships with negative psychosocial stress. Section 1.4 summarises the considerable body of evidence which has examined prospective associations between well-being and cardiovascular outcomes. A brief summary and implications for the thesis are discussed.

### **1.1 Cardiovascular disease and psychosocial risk factors**

#### **1.1.1 The burden of cardiovascular disease**

Cardiovascular disease (CVD) is the leading cause of death worldwide, accounting for an estimated 17.3 million deaths in 2008 (WHO, 2011). Cardiovascular disease is a collective term for a class of diseases affecting the circulatory system. The two most common types of CVD are coronary heart disease (CHD) and stroke. In CHD the vessels supplying the heart are affected by atherosclerosis, a chronic inflammatory process, whilst stroke affects the vessels to the brain (Libby et al., 2009). There were almost 180,000 deaths attributed to CVD in the UK in 2010, of which 80,000 were due to CHD and 49,000 due to stroke. Two thirds of the 46,000 premature deaths from CVD, which includes deaths before the age of 75, occurred in men. CVD mortality rates were higher in more deprived socioeconomic groups, a pattern that has remained relatively stable over the last 15 years (Townsend et al., 2012).

In the UK, and in most developed countries, overall mortality from CVD has been falling for the last fifty years (Scarborough et al., 2011). CHD mortality fell by approximately 6% every year between 2000 and 2007 with about half the decrease due to improved treatment uptake and over 40% due to reductions in major cardiovascular risk factors, particularly reduced blood pressure (Bajekal et al., 2012). Improved survival and a

decrease in new events made similar contributions to annual decreases of over 8.6% in deaths from myocardial infarction (MI) from 2000 to 2010 (Smolina et al., 2012). Recent trends in the rise of obesity and diabetes are slowing the rate of CVD mortality decline (Bajekal et al., 2012).

Despite declining mortality rates, increasing life expectancy and improved survival mean that the economic and social burden of CVD is expected to increase. The estimated annual cost of CVD to the healthcare system in the UK was estimated at £8.7 billion in 2009, the majority of which was due to hospital care and drug prescriptions (Townsend et al., 2012). The prevention of cardiovascular disease is a major public health priority (NICE, 2010).

### **1.1.2 Psychosocial factors influence cardiovascular outcomes**

The most recent public health guidance for the prevention of CVD in the UK identifies smoking, poor diet, hypertension, high blood cholesterol, physical inactivity, obesity, excess alcohol consumption, diabetes and psychosocial stress as modifiable risk factors (NICE, 2010). The relative importance of individual risk factors may vary in different populations, depending on differences in lifestyle, demographics and healthcare provision. For example, the population attributable fraction (PAF)<sup>5</sup> for the effect of smoking on incident non-fatal MI was estimated at 36.4% in an international case-control study of 15,000 patients (Yusuf et al., 2004). The PAF for smoking ranged from 26.1% in North America to 45.5% in the Middle East. In the same study, a composite measure of psychosocial distress derived from depression, perceived status, locus of control, financial status and adverse life events had a similar overall PAF of 32.5%, ranging from 4.9% in Central and Eastern Europe and 51.4% in North America. Accounts of distress in this study were retrospective so may have been biased by the experience of the recent MI, but nonetheless this study indicates that negative psychosocial factors are associated with a significant independent risk of incident CHD (Yusuf et al., 2004).

Psychosocial stressors include negative emotional disorders, such as depression and anxiety, personality traits prone to anger or hostility and chronic exposure to stressful

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<sup>5</sup> The PAF refers to the estimated percentage of potentially avoidable cases of disease that could be avoided if a risk factor was eliminated, assuming a reversible causal association.

conditions (Rozanski et al., 2005; Dimsdale, 2008; Chida and Steptoe, 2009a). Chronic psychosocial stressors linked to the risk of CVD include exposure to adverse conditions in childhood (Nandi et al., 2012), unemployment (Dupre et al., 2012), work-related stress (Kuper et al., 2002a), care-giving (Lee et al., 2003) and marital strain (Eaker et al., 2007). Social isolation has also been identified as an important risk factor for both incident CHD and disease progression (Barth et al., 2010). A meta-analysis of prospective cohort studies published up to December 2011, based on CHD-free populations, found a pooled relative risk for social isolation or loneliness and first CHD event of 1.5 (95% confidence interval (C.I.) 1.2 to 1.9) (Steptoe and Kivimäki, 2013). The same authors conducted a meta-analysis for job strain and reported a relative risk of 1.3 (95% C.I. 1.2 to 1.5) for incident CHD. Adverse psychosocial conditions such as job strain and financial hardship tend to cluster in individuals with lower socioeconomic status and may contribute to the social gradient in CVD (Steptoe and Marmot, 2003).

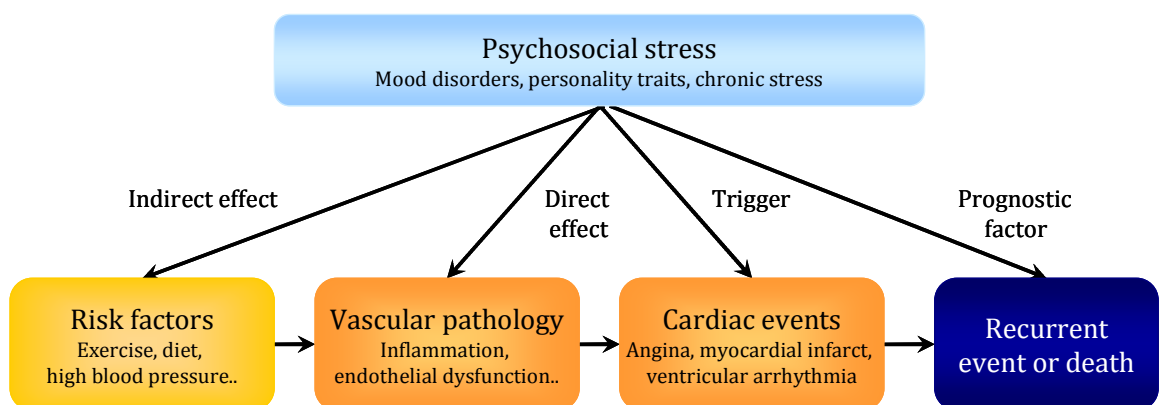
Some individuals are thought to be more vulnerable to the influences of psychosocial stresses than others, owing to inherited or environmental differences. For example, a recent study in the UK suggested that lower socioeconomic status was associated with increased cardiovascular vulnerability to mental distress; depressive symptoms were more strongly associated with CHD and stroke mortality in lower socioeconomic groups (Lazzarino et al., 2013).

There are multiple pathways through which psychosocial factors may influence disease (Figure 1.1). Indirect pathways include influences on health behaviours, such as lower physical activity associated with work stress (Fransson et al., 2012a). Prospective studies evaluating the influence of psychosocial risk factors on incident CVD typically adjust statistically for known behavioural risk factors, implicating direct psychobiological effects on vascular disease processes. For example, a review which summarised evidence from over 138,000 healthy individuals found consistent evidence for an association between depression and incident CHD, which was not explained by behavioural risk factors (Goldston and Baillie, 2008). Heart disease patients with major depression have been estimated to be at more than two-fold risk of further coronary events, taking into account baseline health status (Barth et al., 2004). Non-adherence to medical therapy in

patients with poor mental health may contribute to this association (Bauer et al., 2012), but does not explain disease risks within healthy populations.

Intense negative emotions may also trigger cardiac events (Mittleman and Mostofsky, 2011). Mostofsky et al. (2013) reported that the risk of experiencing acute MI was twice as high after outbursts of anger compared with other times, based on interviews with 4,000 post-MI patients. Studies which rely on patients' retrospective accounts of anger before an event could be influenced by recall bias, as patients seek to explain their heart attack. Ambulatory evidence from patients wearing implantable defibrillators has also shown that that anger is associated with increased ventricular arrhythmias, which can precipitate acute MI (Lampert et al., 2002).

**Figure 1.1 Potential pathways linking psychosocial stress and CVD mortality**  
adapted from Steptoe and Kivimaki (2013)



In addition to the pathways highlighted in Figure 1.1, genetic factors may make individuals with mental health problems, or exposed to certain environmental stressors, more prone to develop CVD. One study in over 30,000 twins found that although major depression and CHD shared common genetic antecedents, the genetic correlation was relatively small. The authors concluded that environmental effects played a more dominant role, particularly in men and older subjects (Kendler et al., 2009). Genetic pathways and are not currently amenable to intervention and will not be investigated in this thesis. In Chapter 2, I will discuss psychobiological mechanisms in more detail.

### *Is there a role for 'protective' psychosocial factors?*

In one sense, the evidence outlined in section 1.1.2 above supports the case to investigate psychological well-being and cardiovascular disease; there is a strong case for psychological influences on aetiology and prognosis. But if positive psychosocial characteristics only reflect the absence of stressful conditions or negative mood disorders, there is a risk of simply re-framing existing evidence. For example, there is a literature which focuses on the protective effects of social support and social networks on cardiovascular outcomes which might arguably be re-framed in terms of the increased risks associated with social isolation (Kawachi et al., 1996; Holt-Lunstad et al., 2010). In section 1.2, I discuss how to define and measure well-being. Section 1.3 reviews what is known about how well-being is related to negative psychosocial risk factors for CVD.

## **1.2 Defining and measuring subjective well-being**

In this thesis, well-being refers to subjective well-being, where people are asked to assess their own thoughts and feelings about how well their lives are going. There are three main approaches to the assessment of subjective well-being: evaluative, hedonic and eudemonic measures (Dolan et al., 2011).

### **1.2.1 The life evaluation approach, a cognitive assessment**

Evaluative measures of well-being involve an overall summary assessment of life satisfaction, or general happiness. For example, the Satisfaction With Life Scale includes 5 statements, such as 'In most ways my life is close to my ideal', rated on a 7-point agree-disagree scale (Diener et al., 1985). Evaluative accounts require cognitive judgements to be made about how someone thinks and feels compared to their desired status. Evaluative measures are easily comprehensible and are widely used in national and international surveys (Waldron, 2010). For example, the European Social Survey asks 'All things considered, how satisfied are you with your life as a whole nowadays?' and 'Taking all things together, how happy would you say you are?' each on a scale of 0 to 10. When referring to the same time span and response scale, responses to these evaluative measures of life satisfaction and general happiness are very highly correlated to one another (Helliwell et al., 2012). Evaluative measures may not be sensitive to changes in well-being associated with daily activities or environmental influences (Knabe et al.,



2010), suggesting that a more nuanced approach to well-being is needed. Retrospective evaluations of happiness have also been criticised because they can be influenced by peak experiences and recent mood, as discussed below (Kahneman et al., 2006).

### **1.2.2 Hedonic well-being, the experience of pleasure**

The origins of hedonism can be traced back to Aristippus, a Greek philosopher who argued that the goal of life is to experience maximum pleasure (Ryan and Deci, 2001). Utilitarian philosophers, such as Jeremy Bentham, advanced the view that moral actions should result in the greatest happiness for the greatest number of people. Bentham defined happiness as a predominance of pleasure and the absence of pain (Sweet, 2001).

Hedonic psychology has been defined as the study of “what makes experiences and life pleasant and unpleasant” (Kahneman et al., 1999). Hedonic experience may therefore include both positive and negative affect. Positive affect can be defined as the feelings or emotions that reflect a state of pleasurable engagement with the environment such as happiness, joy, enthusiasm and contentment (Tomkins, 1963). Negative affect refers to distressed or unpleasant mood states such as anger, sadness, fear and anxiety. In this thesis, positive affect is used as an umbrella term for positive emotions and positive moods (Kristjánsson, 2012).<sup>6</sup>

The most widely used measure of affect is the 20-item Positive and Negative Affect Schedule, PANAS (Watson et al., 1988). Respondents are asked to rate the extent to which they feel, or have felt, a list of positive (e.g. interested, enthusiastic, strong, attentive) and negative (e.g. distressed, scared, irritable, upset) adjectives over a specified time frame. Affect rating scales such as the PANAS have been shown to have good construct validity and re-test reliability. In fact, the stability of affect ratings over time suggests that repeated measures can be used as trait or dispositional measures of affect (Watson et al., 1988; Pressman and Cohen, 2005).

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<sup>6</sup> Some authors distinguish between measures of affect, mood and emotion. For example, Kristjánsson (2002) describes moods as objectless states and emotions are as having intentional objects: they are *about* something. However widely used measures of affect, such as the PANAS, do not allow a distinction between the two, so the terms are used interchangeably in this thesis. For a more detailed discussion of affect, mood and emotion, see Ekkekakis (2013).

Possible reference time scales for the PANAS include present moment (now), day (today or yesterday), past few days, week, past few weeks, year and 'in general'. Affect rating scales which refer to current or very recent experience, such as 'right now', or today, are measures of hedonic experience but when respondents are asked to consider their general mood, it could be argued that this is an evaluative measure (Waldron, 2010; Dolan et al., 2011). There does not appear to be a consensus about reference time-scales for positive affect which separate hedonic versus evaluative measures; responses could be thought of on a continuum from experienced hedonic affect ('how do you feel now/how have you felt today') to a more evaluative end of the spectrum ('how have you felt over last month/year').

Some authors do not acknowledge a distinction between measures of momentary hedonic experience and evaluative well-being, grouping all responses to positive affect rating scales as hedonic well-being or positive affect e.g. (Lyubomirsky et al., 2005a; Boehm and Kubzansky, 2012). A limitation of assessing hedonic well-being retrospectively is that there is a discrepancy between recalled evaluations of emotional experience ('life as we remember it') and the mean of experienced emotions over a given time period ('life as we live it') (Miron-Shatz et al., 2009). For example, memories of intense pain are often exaggerated in retrospective evaluations (Kahneman et al., 1993). This discrepancy has been characterised as the 'memory-experience gap' (Miron-Shatz et al., 2009). Explanations for the gap include salience memory heuristics, in which there is an over-reliance of memory on specific instances, such as peak or prominent experiences (Stone et al., 2005). Personal theories about typical events, such as a 'rosy view' of holidays, can also introduce a recall bias in retrospective evaluations of a single event (Wirtz et al., 2003). Forgas' (1995) Affect Infusion Model suggests that extensive processing of information increases the influence of local or current emotions on responses. The memory-experience gap tends to be more pronounced for negative emotions; people typically remember being more angry or sad than their momentary experiences suggest (Miron-Shatz et al., 2009).

Ecological momentary assessment (EMA, also the experience sampling method) was developed to minimise the potential for recall and heuristics biases by collecting information on people's feelings in real time in natural settings during selected moments

of the day (Csikszentmihalyi and Larson, 1987; Stone and Shiffman, 2002). Assessments of affect repeatedly over many days can more accurately account for within-person variability in affect than single measures (Bolger et al., 2003). However, the time burden of multiple assessments could be a deterrent for research participants. The Day Reconstruction Method (DRM) was designed to reduce recall biases by eliciting careful reconstruction of timed episodes over the day. Participants are asked to recall their moods separately for each episode. Subjective assessments of feelings can be weighted by duration to derive a 'hedonic calculus' for each episode or activity and ultimately a person's affective profile for an entire day (Kahneman et al., 2004). Analyses comparing emotional memories using DRM and EMA and has shown that DRM provides reliable estimates both of the intensity of affect and variations in affect over the day (Dockray et al., 2010).

*Is positive affect the opposite of negative affect?*

Factor analyses of mood ratings conducted across different populations suggest that positive and negative affect are two independent unipolar dimensions (Diener and Emmons, 1984; Watson and Tellegen, 1985). Positive and negative affect are typically inversely correlated but statistically independent; that is, positive affect does not reliably predict negative affect, e.g. (Bradburn, 1969; Watson et al., 1988; Cacioppo and Berntson, 1994). It has been suggested that the degree of correlation may depend on the time frame, with longer reference durations being associated with more independent ratings (Diener and Emmons, 1984) but this is not always the case (Watson, 1988).

An opposing model of emotions, proposed by Russell (1980), argued that pleasant and unpleasant emotions represent opposite ends of a unipolar 'valence' dimension. A second dimension, 'activation' or 'arousal', can be represented as a vertical axis intersecting the horizontal valence axis. Using this circumplex model, happiness (pleasant-activated) is diametrically opposed to sadness (unpleasant-deactivated), indicating that the two are mutually exclusive. Russell and Carroll (1999) argued that positive and negative affect cannot be opposites, since correlations rarely approach -1. The more typical correlation of around -0.4 could be consistent with mutual exclusivity.

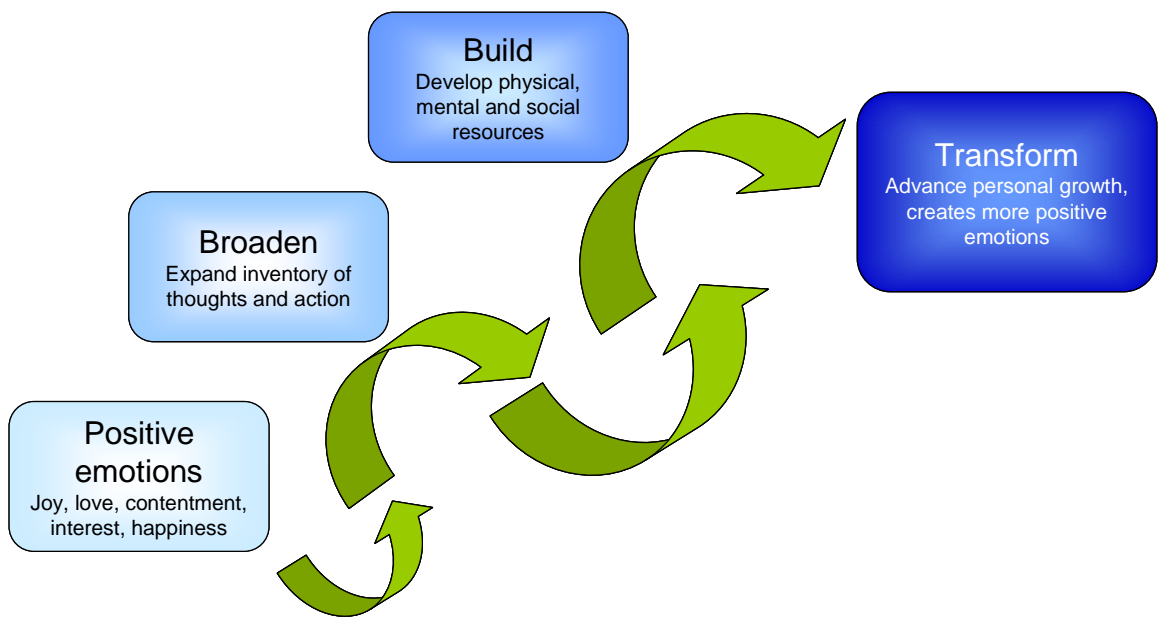
Despite some empirical support for the circumplex model (Posner et al., 2005), there is compelling evidence that positive and negative affect can be treated as separate

constructs. EMA affect ratings over the day indicate that negative emotions such as stress/tension do not mirror the diurnal rhythm of happiness, which tends to increase over the latter part of the day (Kahneman et al., 2004). Happiness and tiredness show a similar diurnal pattern, intuitively contrary to the circumplex theory that happiness is associated with arousal (Stone et al., 2006). It has also been shown that negative and positive affective states can be reported simultaneously, even 'diametric opposites' such as happiness and sadness (Larsen et al., 2001; Rafaeli and Reville, 2006). A more prominent and persistent memory-experience gap for negative emotions versus positive emotions has also been used as an argument to support separate neural paths for emotions of positive and negative valence (Isen, 1999; Miron-Shatz et al., 2009). Functional neuro-imaging studies suggest that both trait and state measures of positive and negative affect are associated with asymmetrical activation in the prefrontal cortex, which may indicate distinct neural mechanisms of control (Davidson, 2004). Further examples of independent biological associations will be discussed in Chapter 2. Positive and negative emotions may also have evolved to enable organisms to perform very different functions, as proposed by the broaden-and-build theory (Fredrickson, 2001).

#### *Broaden-and-build theory of positive emotions*

From an evolutionary perspective, negative emotions are thought to function as a rapid response to threat, narrowing attention towards specific actions such as fight or flight (Frijda, 1988). In contrast, positive emotions arise in conditions of safety and desirability, signifying that life is going well and resources are adequate (Carver, 2003). Fredrickson (1998; 2001) proposed that positive emotions also have an adaptive value in preparing the organism for future challenges. The broaden-and-build theory posits that positive emotions broaden an individuals' thought-action repertoire (attention, working memory, openness to information). Positive cognitions promote proactive behaviours which enable individuals to expand their resources and friendships, lead to a self-reinforcing 'upward spiral' (Figure 1.2). The theory also states that positive emotions 'undo' the physiological effects of negative emotions.

**Figure 1.2** Positive emotions may lead to a positive cycle of enduring well-being  
adapted from Garland et al. (2010a)



Much of the early empirical evidence to support the theory was based on experiments to induce positive or negative feelings in student subjects (e.g. by showing sad or happy film clips) and subsequently measuring performance, CV function or psychological well-being (see 1.2.3 below) (Fredrickson and Levenson, 1998; Fredrickson and Branigan, 2005). Laboratory manipulations may not generalise to real-life. Furthermore, although two studies supported a faster CV recovery to stress following films designed to induce amusement or contentment than sadness or fear (Fredrickson and Levenson, 1998; Tugade and Fredrickson, 2004), other similar studies found no significant differences in cardiovascular responses that were unique to positive affect manipulation (Fredrickson et al., 2000; Gendolla and Krusken, 2001). Evidence to support the theory that positive emotions build subsequent psychological resources included observations from studies showing that baseline ratings of positive affect were associated with coping, resilience and mental flourishing several months later (Fredrickson and Joiner, 2002; Fredrickson et al., 2003). Such associations, based on self-reported questionnaires, might all be related to a trait-like positive outlook (discussed in section 1.3i below), yet the influence of stable dispositional traits received little attention in the original theory.

A more direct test of the 'build' theory used Loving-Kindness Meditation to provoke feelings of warmth and caring for self and others. Meditation was associated with increased daily ratings of positive emotions over nine weeks. Path analyses showed that increases in positive emotions predicted gains in psychological resources such as purpose in life, which predicted increased life satisfaction (Fredrickson et al., 2008a). It is difficult to test whether positive emotions *caused* improvements in psychological health, or whether increased positive affect was a 'symptom' reflecting increasing psychological well-being. The extent to which the broaden-and-build theory is empirically testable versus an a priori truth was questioned in an unpublished thesis by (Snaebjörnsdóttir, 2010), cited by (Kristjánsson, 2012). For example, regarding the 'undoing' effect of positive emotions on negative emotions, Snaebjörnsdóttir argued that it is true a priori that persons who consciously report positive emotions such as hope or happiness will think and act in differently to those who maintain negative feelings; one would not expect persons feeling hopeful and hopeless to think and behave in the same way. Whether or not it is appropriately labelled as a 'theory', the broaden-and-build model has been widely cited in the psychological literature, with over 1,400 citations in Web of Science.<sup>7</sup> It provides a useful reminder that the conscious experiences of positive versus negative affect can be associated with different cognitions and behaviours.

### **1.2.3 Eudemonic well-being, positive mental functioning**

From a eudemonic perspective, the experience of happiness as pleasure is not a sufficient condition for well-being (Ryan and Deci, 2001). Eudemonia, based on the philosophy of Aristotle, is a condition associated with living a life of contemplation and virtue. Most modern concepts of eudemonic well-being focus on psychological characteristics which are thought to represent optimal functioning, or flourishing. Jahoda (1958) is often attributed with the first definition of 'positive mental health' (Huppert and So, 2013). Based on clinical and personality theorists' perspectives on positive functioning, she identified six elements of positive functioning: attitudes of an individual towards themselves, self-actualisation, integration, autonomy, perception of reality and environmental mastery. Alternative attempts to define eudemonia have referred to the feelings of doing 'something worth doing' (Norton, 1976); growth, purpose and being true

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<sup>7</sup> Citations for Fredrickson (2001), the original description of the broaden-and-build theory in American Psychologist, according to Web of Science July 2013

to one's self or fulfilling one's potentials (Waterman, 1993) and sense of coherence, in which life is seen as comprehensible, manageable and meaningful (Antonovsky, 1993).

Two theoretical developments have helped integration of eudemonic concepts into large-scale population studies. Firstly, Ryff and Keyes created a multidimensional model of Psychological Well-Being (PWB), influenced by Jahoda and theoretical perspectives from clinical and developmental psychology (Ryff, 1989; Ryff and Keyes, 1995). The authors identified six psychological resources they felt were required to flourish throughout the lifespan. The six dimensions of PWB are: self-acceptance (feeling good about oneself even whilst aware of one's limitations), positive relations (warm and trusting interpersonal relationships), environmental mastery (ability to shape one's environment so as to meet personal needs and desires), autonomy (self-determination and authority), purpose in life (finding meaning in one's efforts and challenges) and personal growth (making the most of one's talents and capacities).

Self-determination theory (SDT) (Ryan and Deci, 2000) is another influential approach related to eudemonia which has influenced recent well-being assessment (Michaelson et al., 2009; ONS, 2012). SDT was developed as a theory of motivation, concerned with how to support natural or intrinsic tendencies to behave in effective and healthy ways. Three basic psychological needs are proposed as the 'nutrients' or necessary conditions for effective psychological functioning: autonomy (to be able to control one's life and act in line with one's goals), competence (to experience mastery, confidence) and relatedness (to be connected to others). These basic conditions overlap with PWB dimensions. SDT conceptualises the three basic needs as factors from which well-being will arise, whereas Ryff suggests that the PWB scale is a measure of eudemonic well-being.

#### **1.2.4 Towards a consensus: well-being as a multidimensional construct**

Positive psychology emerged within the last two decades as 'the scientific study of optimal human functioning' (Seligman and Csikszentmihalyi, 2000). Diener, a prolific author in this field, argued in 1999 that eudemonic constructs could be criticised as external judgements of what should constitute optimal functioning, rather than an individual's own perspective (Diener et al., 1999). At that time, subjective well-being was often assessed using a combination of satisfaction with life (evaluative well-being) and the balance of positive

and negative affect (hedonic well-being) (Diener, 2000). Life satisfaction, happiness and composite measures of positive affect tend to load on a single dimension in factor analyses (Slocum-Gori et al., 2009), so the terms were often referred to interchangeably.

Proponents of eudemonic well-being challenged evaluative measures for being of limited scope and failing to indicate healthy living (Ryff, 1989; Waterman, 2008). One key difference between perspectives is in the type of activities and goals that may promote well-being (Ryan and Deci, 2001). Waterman (1993) argued that activities to promote eudemonic well-being must be valued for their own sake, involve effort and self-realisation. For example, Nix and colleagues (1999) showed that succeeding at an activity whilst being forced to do so resulted in happiness, but not vitality, which was argued to be integral to eudemonia. White and Dolan (2009) used ratings of affect and time use over the day to show that work was the activity associated with the lowest ratings in terms of positive emotion, but ranked highest in terms of psychological rewards (competence, engagement and achievement of goals).

Interest in the assessment of subjective well-being to guide public policy, both in the UK and internationally, has led to considerable efforts to reach a consensus towards definitions and measurement (Dolan et al., 2011; OECD, 2011). It is now widely accepted that evaluative, hedonic and eudemonic constructs all contribute to understanding an individual's well-being. For example, Seligman, one of the early proponents of positive psychology, initially claimed that 'authentic happiness' was composed of three subjective facets: positive emotion, engagement, and meaning (Seligman, 2002). Seligman (2011) subsequently revised this theory to redefine the endpoint as 'well-being', in order to stress the multifaceted nature of human flourishing, and expanded it to include positive relationships and accomplishment (eudemonic constructs). Diener (2010) similarly broadened earlier measurements of subjective well-being to add the concept of flourishing, including: purpose in life, positive relationships, engagement, competence, self-esteem, optimism and contributing to the well-being of others.

In the UK, after a public consultation about the nature of well-being, the Office of National Statistics introduced four core subjective well-being questions and a number of additional eudemonic statements into the ONS Opinions Survey, a nationally representative panel survey. The core questions assessed life satisfaction (evaluative



approach), feelings of happiness and anxiety yesterday (hedonic experience approach) and to what extent respondents feel the things they do in their life are worthwhile (eudemonic approach). Initial results revealed that most were happy most of the time: in the UK mean happiness yesterday was  $7.4 \pm 0.09$  (Table 1.1). Experienced happiness was positively correlated with life satisfaction ( $r=0.55$ ) and worthwhile activities ( $r=0.51$ ) and negatively associated with anxiety ( $r=-0.39$ ). Correlations with eudemonic constructs were stronger for life satisfaction than experienced affect. None of the eudemonic constructs were associated with anxiety yesterday ( $r<-0.3$ ). A review of pilot data concluded that all four statements assessed distinct aspects of well-being and should be retained in on-going surveys (ONS, 2012).

**Table 1.1**      **Average ratings for subjective well-being (ONS, 2012)**  
Great Britain, adults aged 16 and over

	Mean	Mode	Median
Core questions			
Life satisfaction	7.4	8	8
Worthwhile activities	7.6	8	8
Happiness yesterday	7.4	8	8
Anxious yesterday	3.4	0	3
Eudemonic statements (examples)			
How well do you generally get on with people around you?	8.4	-	-
How positive do you feel about yourself as a person?	7.6	-	-
Do you feel a sense of accomplishment from things you do in your daily life?	7.3	-	-

Interestingly, although ‘subjective’ well-being by definition is an individual assessment of one’s own feelings, external perceptions of well-being have been linked to similar outcomes (Harker and Keltner, 2001; Davidson et al., 2010). In a study of 196 students, there was similarly high consistency between evaluative measures and PWB (eudemonic) with acquaintance and clinician ratings of personality characteristics and directly observed social interactions (Nave et al., 2008). There is therefore some evidence that it may be valid to combine different aspects of well-being within a single measure. For example, the Warwick Edinburgh Mental Well-being Scale (WEMWBS) was developed to

capture a broad concept of positive mental well-being including psychological functioning, cognitive-evaluative dimensions and affective-emotional aspects (Tennant et al., 2007). The 14-item positively worded scale is relatively short and does not suffer from ceiling effects, making it suitable for use in large-scale population surveys. WEMWBS was introduced into the Health Survey for England, a nationally representative annual population survey, in 2010 (Bryson et al., 2011). I use WEMWBS to assess well-being in the intervention described in Chapter 8. The extent to which different dimensions of subjective well-being have different associations with cardiovascular outcomes will be discussed in section 1.4.

### **1.3 Determinants, correlates and consequences of subjective well-being**

As I mentioned in the introduction, global policy makers are increasingly looking to measures of subjective well-being as useful and sustainable indicators of societal progress (Stiglitz et al., 2009). Considerable research has therefore been conducted at both between-country and within-country level with the aim of identifying potential policy levers to promote well-being (Dolan et al., 2008; Blanchflower and Oswald, 2011). To date much of this research has been cross-sectional, which limits causal inferences, but there is increasing interest in the longitudinal direction of associations (Luhmann et al., 2012). This section highlights those variables which have been consistently associated with well-being across multiple studies and which are relevant to cardiovascular disease risk. The factors are: genetic factors, sociodemographic characteristics, physical health, health-related behaviours, chronic stress and depression. A more comprehensive review of the correlates of well-being is available elsewhere e.g. (Helliwell et al., 2012). Before considering the evidence for prospective associations between well-being and CVD outcomes, it is important to identify those factors which could be confounders (such as baseline physical health) or could be on the causal pathway to disease; either as antecedents of well-being (such as socioeconomic status) or downstream mediators (such as health-related behaviours).

#### *i) Genetic factors and personality*

Studies of U.S. twins have estimated that one-third to one-half of within-country variance of happiness can be explained by genetic differences between individuals (Lykken and Tellegen, 1996; De Neve et al., 2012). A recent study based on estimates of 'narrow

heritability', the fraction of variance in subjective well-being accounted for by the cumulative additive effects of all genetic polymorphisms, suggested that heritability was lower at 12-18% (Rietveld et al., 2013). Twin studies suggest that common genes link subjective well-being and personality (Weiss et al., 2008). Of the Big Five personality traits, meta-analyses by DeNeve and Cooper (1998) and Steel et al. (2008) found that positive affect was positively associated with extraversion and happiness and life satisfaction were inversely associated with neuroticism. A study examining the genetic architecture of eudemonic well-being suggested that substantial genetic influences were underpinned by a single factor influencing self-control (Archontaki et al., 2013). The strength of association between well-being and negative personality traits linked to CVD outcomes appears to be relatively weak; for example, in a study of over 500 students, correlations with the specific facet of hostility were  $r = -0.20$  for happiness,  $-0.19$  for life satisfaction and  $-0.13$  for positive affect (all  $p < 0.01$ ). Happiness and the personality facet of optimism were more strongly positively correlated ( $r = 0.49$ ) (Marrero Quevedo and Carballeira Abella, 2011).

#### *ii) Sociodemographic characteristics*

Table 1.2 lists associations between social, demographic and health variables and life satisfaction over time from the British Household Panel Survey (1996-2008), highlighting how these results compare with other studies.

The extent to which income predicts well-being at a country level has been subject to considerable debate (Easterlin, 1974; Sarracino, 2013), but in cross-sectional surveys at an individual level, low income is typically associated with low subjective well-being (Blanchflower and Oswald, 2011). The strongest relationships are with self-reported health (discussed in point iii below) and with being separated or widowed. Overall, the model accounts for less than 10% of the variance in life satisfaction, suggesting that age, socioeconomic status, social relationships and self-reported health are relatively weak predictors of well-being. This is consistent with analyses of happiness correlates based on data from the United States (Blanchflower and Oswald, 2011).

**Table 1.2 Fixed effects regressions to explain life satisfaction from the British Household Panel Survey, BHPS (1996-2008)**

A U-shaped association between **age** and evaluative well-being is often seen in the US and UK (though not significant here) (Blanchflower and Oswald 2008). Eudemonic constructs may be more variable: meaning in life increases with age (Steger et al. 2009) while personal growth tends to decline in older age (Ryff et al. 2004).

Cross-sectional studies consistently find a negative association of **unemployment** on life satisfaction, and a positive effect of **self-employment** (Dolan et al. 2008).

On average across studies, the presence of **children in the household** is not associated with higher life satisfaction. Level of **education** also has no clear direct impact on happiness, but is indirectly related to happiness through its effect on income (Helliwell et al. 2012)

BHPS	
Log of income (monthly)	0.13*
Female	--
Age	-0.08
Age^2/1000	0.56
Single	0.13*
Widowed	-0.18*
Divorced	-0.14*
Separated	-0.34*
Unemployed	-0.22*
Self Employed	0.01
Out of the labour force	-0.12*
Student	0.07
Education: High	-0.07
Education: Medium	0.13*
One child	0.01
Two children	0.03
Three + children	0.06*
Health	
Excellent	1.04*
Good	0.90*
Satisfactory	0.64*
Poor	0.36*
Fixed effects	Yes
Time Dummies	Yes
Region Dummies	Yes
Observations	53615
R <sup>2</sup>	0.09

\*p<0.05

In most developed countries **women** report slightly higher satisfaction than men, but also higher levels of mood disorders; in cross sectional analysis of BHPS, female sex had a significant weak regression coefficient (0.09) for life satisfaction (Helliwell et al. 2012).

**Social contact and relationships** have a stronger positive association with well-being than income or demographic factors (Diener et al. 1999). Marriage is typically associated with higher levels of well-being than cohabiting or being single, but the lowest levels are reported after divorce or separation (ONS 2012).

**Self-rated health** has a similar graded association with eudemonic, hedonic and evaluative well-being in cross-sectional studies (ONS 2012). Objective health indicators are less strongly associated with well-being, perhaps reflecting individual differences in resilience (Angner et al. 2009).

Fixed effects for each individual and year are included so that the equation estimates the effect of each variable in explaining the different levels of happiness which an individual experiences in each different year. Adults aged 30-55. Table extracted from the World Happiness Report, p85 (Helliwell et al., 2012)

Associations between socioeconomic characteristics and well-being may be bidirectional. A longitudinal study of British lottery winners found that wins between £2,000 and £120,000 were associated with small but significant increases in mental well-being two years later compared with non-winners (Gardner and Oswald, 2007). Conversely, data from a nationally representative US panel survey showed that adolescents who reported higher levels of positive affect or life satisfaction earned higher salaries ten years later. Predictive effects of positive affect were robust to adjustments for family effects (sibling clusters), education, intelligence quotient, physical health, height, self-esteem and later happiness. The authors identified a higher probability of obtaining a

college degree, getting hired and promoted, having higher degrees of optimism and extraversion, and less neuroticism as mediating pathways (De Neve and Oswald, 2012).

It is important to note that a weak U-shaped association between well-being and age may change in the final years of life. Gerstorf et al. (2010) showed using data from the UK, Germany and the US that well-being declined rapidly within the final 3 to 5 years of life. This observation was not adjusted for physical health, so may simply reflect failure to adapt to worsening physical health. Longitudinal analysis of panel data based over 23,000 German adults aged 17 to 85 followed up over five years supported a U-shaped pattern in life satisfaction aged 20 to 70, with peaks at around 23 and 69, and a decline from age 75 years (Schwandt, 2013). This analysis did not control for health status.

### *iii) Physical health*

As suggested in Table 1.2, poor self-reported physical health is associated with worse well-being. Longitudinal analysis of the British Household Panel Survey over 6 years suggested that this association is not simply explained by a negative response bias (Oswald and Powdthavee, 2006). Overall, those who reported being disabled every year (n=129) had life satisfaction almost one standard deviation lower than those who remained able bodied (n=13,776). Reporting a disability for the first time was associated with a reduction of approximately half a standard deviation from an individual's pre-disability level. There was evidence of adaptation to disability, such that one year later, approximately half of the effect of disability had dissipated. These changes were not substantially reduced by adjustments for economic and demographic factors but the authors noted that there was considerable variation in the effects on life satisfaction. A comparison of quality of life across older adults with chronic conditions found lowest levels in those with stroke and least impairment for cancer and diabetes (Wikman et al., 2011).

### *iv) Health-related behaviours*

Boehm and Kubzansky (2012) reviewed the evidence for associations between behaviours associated with increased cardiovascular risk and aspects of well-being. Few longitudinal studies were identified but there was strong cross-sectional evidence to support a link between subjective well-being and physical activity, good sleep quality and adequate sleep quantity, reduced risk of smoking and a healthy diet. Generally links with optimism and

evaluative measures of well-being were more consistent than for eudemonic well-being. A recent longitudinal study of over 10,000 young adults found that general well-being in adolescence predicted fewer risky health behaviours 15 years later, after adjusting for baseline behaviours and depressive symptoms (Hoyt et al., 2012). The behaviours were eating fast food, binge drinking, smoking, taking drugs and physical inactivity. However, one study which measured daily affect and lifestyle behaviours over four weeks in over 400 middle-aged workers found that negative affect was more consistently associated with unhealthy behaviours that day than positive affect (Jones et al., 2007). For example, negative affect was linked to smoking, higher consumption of alcohol and high-fat snacks in men whereas positive affect was only significantly associated with higher alcohol. It is not clear from this study whether affect preceded behaviour, or vice versa.

Increased physical activity has also been prospectively linked to increased positive affect, suggesting a bidirectional association between well-being and some health behaviours (Baker et al., 2008). One dietary modification trial suggested that women with higher baseline levels of optimism were more likely to adhere to a healthier diet one year later (Tinker et al., 2007). A study in cardiac transplant patients also found that baseline optimism about the forthcoming operation predicted greater adherence to post-transplant medication regimen 6 months later (Leedham et al., 1995). Several studies in HIV patients also identified a cross-sectional association between positive affect and self-reported adherence to medication (Sherr et al., 2008; Carrico et al., 2010). In contrast, a more thorough analysis which controlled for regimen complexity found that positive affect no longer predicted adherence after adjusting for AIDS stage and symptoms: patients in symptomatic stage were more likely to adhere to medication (Reis et al., 2013). Effects reported in previous studies may have been confounded by treatment side effects; in the analysis by Ries et al., participants who reported no treatment side effects reported both higher adherence and higher positive affect.

#### *v) Chronic psychosocial stress*

Stressful life events may have effects on well-being that are independent of socioeconomic status. Herrenkohl et al. (2012) identified a low to moderate correlation ( $r < 0.30$ ) between maltreatment in childhood, based on child welfare records, and measures of autonomy, happiness and life satisfaction in adulthood, after adjusting for childhood socioeconomic status. Wide variation in the extent to which an individual's well-being adapts to adverse

events over time has been reported, but evidence from prospective studies suggests that life satisfaction is typically lower following divorce or unemployment (Lucas et al., 2004; Lucas, 2005). A negative influence of chronic stressors on well-being may be moderated by a number of factors related to the stressor or the individual. For example, Raina et al. (2005) found that the well-being of care-givers of children with cerebral palsy depended on perceived care-giving demands, child behaviour problems, individual self-perception and use of stress-management techniques. Luhmann et al. (2012) conducted a meta-analytic review of 188 longitudinal studies examining the association between life events (marriage, divorce, bereavement, childbirth, unemployment, re-employment, retirement, relocation) and affective/hedonic and evaluative measures of well-being. Effects tended to be stronger for cognitive or evaluative measures such as life satisfaction than affective measures. The review concluded that life events can have very different effects on affective and evaluative well-being measures which vary by event and are not a direct function of the alleged desirability of events.

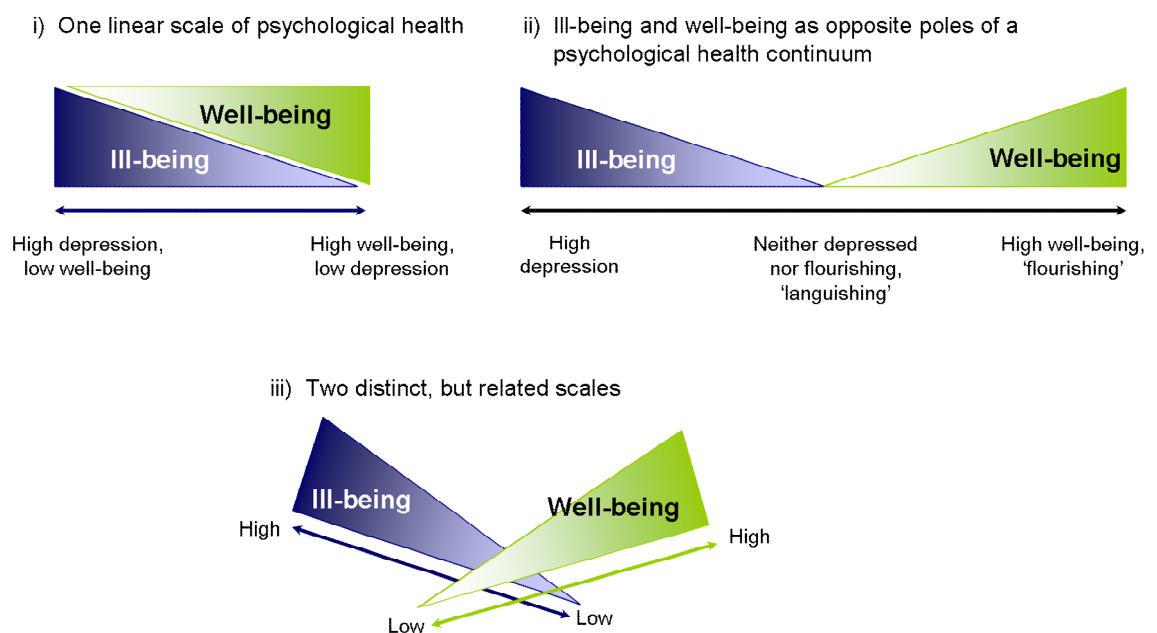
To date less attention has been paid to prospective relationships from baseline well-being to negative psychosocial exposures. A review by Lyubomirsky et al. (2005a) suggested that higher dispositional positive affect was associated with successful outcomes across a number of domains, including marriage, income, employment and work performance, but acknowledged that longitudinal studies which controlled for baseline socio-economic circumstances were scarce. Recent analyses of three nationally representative samples from Australia, Germany, and Great Britain suggested that people reporting greater satisfaction with life were more likely than dissatisfied people to get married or become parents in the next 5 years, and less likely to divorce, lose their job, start a new job, or relocate in the next 5 years (Luhmann et al., 2013). These effects were consistent across countries and held after controlling for gender, age, income, education, and the Big Five. A small study predicting coping and mood following surgery for breast cancer showed that pre-existing levels of positive mood predicted the tendency to cope through humour, positive reframing and active engagement, resulting in lower psychological distress (Carver et al., 1993).

*vi) Mood disorders, such as anxiety and depression*

Figure 1.3 shows three alternative relationships between well-being and depression: i) low well-being as equivalent to depression; ii) opposite ends of a single psychological

health dimension; iii) two distinct, but inversely related measures. The diagnostic criteria for depression includes loss of pleasure or anhedonia, in addition to persistent sadness/low mood, fatigue and symptoms such as disturbed sleep, poor concentration and suicidal thoughts (NICE, 2009). It is therefore unsurprising that depressive symptoms and positive affect are typically inversely correlated, but positive mood is only one indicator of subjective well-being.

**Figure 1.3 Potential relationships between mental ill-being and well-being**



Functional MRI evidence suggests that patients with major depression can experience positive affect, but are unable to sustain it for as long as healthy adults (Heller et al., 2009). Population studies report that depressive symptoms and eudemonic and hedonic measures of well-being have only moderate inverse correlation coefficients (Keyes, 2002). It is therefore unlikely that 'low well-being' is equivalent to 'high ill-being' or depression, represented by Figure 1.3i).

It is possible to report both low depressive symptoms and low well-being, giving rise to the idea of a single mental health continuum (Figure 1.3ii), whereby individuals may be 'languishing' without symptoms of mental ill-health but failing to flourish (Keyes, 2002; Huppert, 2009). Based on this idea, Huppert and So (2013) developed a new



measure of well-being based on positively worded statements that were the opposite of each internationally agreed symptom for depression and anxiety. The 'flourishing scale', which included both hedonic and eudemonic components, had low correlations with life satisfaction, suggesting a distinction between these concepts (overall  $r < 0.34$ ,  $p < 0.01$ ) (Huppert and So, 2013).

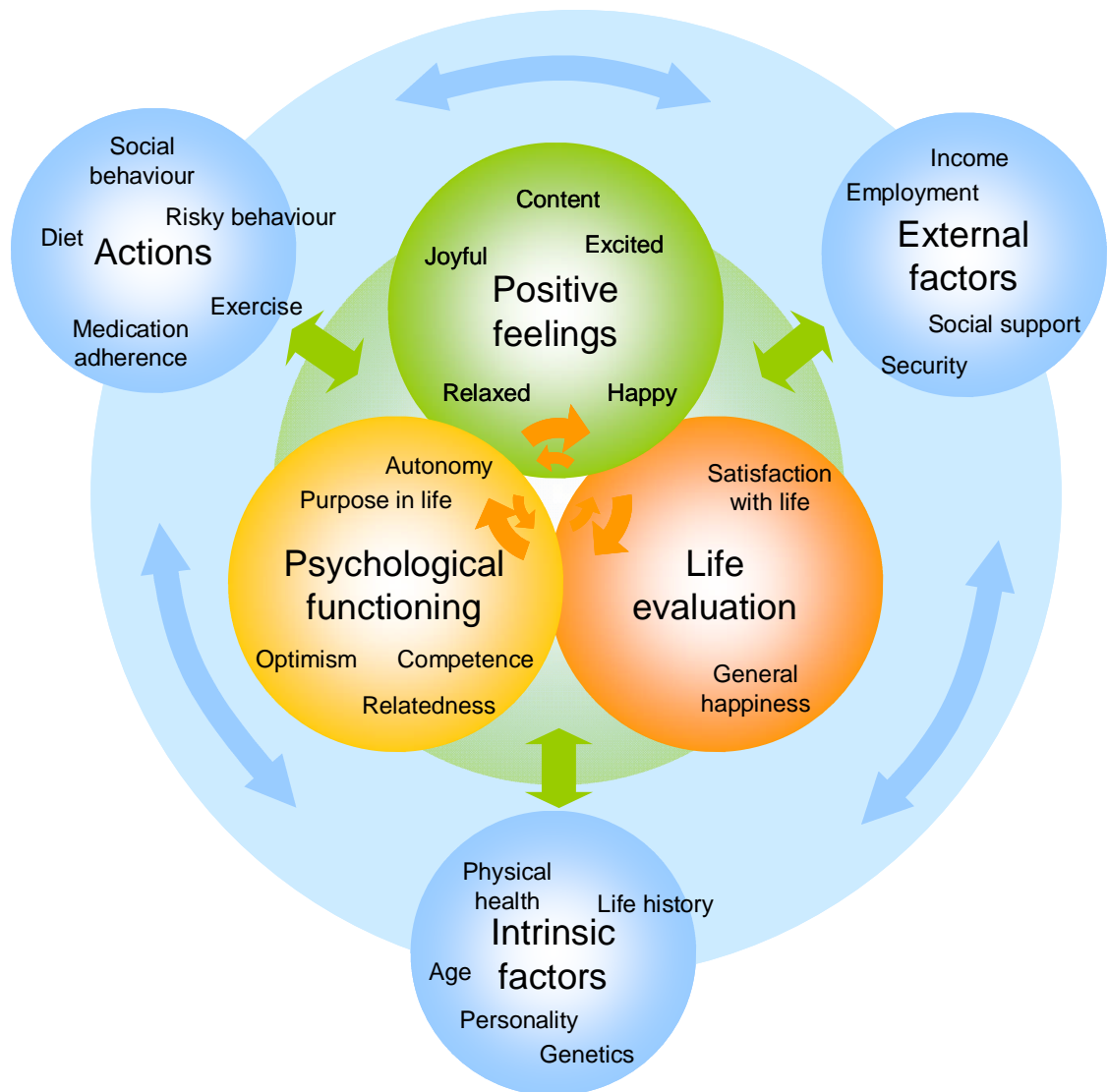
Well-being and ill-being may be two distinct but inversely related constructs (Fig 1.3iii), similarly to positive and negative affect, with independent effects. Well-being could therefore be protective against later depression. For example, a longitudinal study within over 5,000 older adults aged 51-56 years showed that high eudemonic well-being was associated with reduced risks of depression 12 years later, after adjustment for personality, negative functioning, prior depression, physical health and sociodemographic variables (Wood and Joseph, 2010). Evidence for independent effects of positive and negative affect on biological outcomes will be discussed in Chapter 2.

#### *Summary of section 1.2: a working model of well-being*

Well-being can be defined as a multi-dimensional construct which includes experienced positive affect (hedonic experience), cognitive evaluations of life circumstances (evaluative well-being) and positive psychological functioning (eudemonic well-being). I propose that all three of these core areas are indicators of subjective well-being. According to the broaden-and-build theory and self-determination theory these factors interact in a dynamic way, such that positive emotions influence positive life evaluations and eudemonic attributes such as autonomy and control, and vice versa (Figure 1.4). It has been shown that the frequency and duration of positive experience predict evaluative well-being to a greater extent than intensity (Diener et al., 2009).

**Figure 1.4 A dynamic model of well-being**

Model inspired by Thompson and Marks (2008), Fredrickson (2001), Ryan and Deci (2000), Lyubomirsky et al. (2005a)



I suggest that external resources (material, social and environmental factors), personal resources and experience (genetics, personality traits, education) and health-related actions or behaviours can all interact with well-being in a bidirectional fashion. Optimism is the general perception that future positive outcomes will be more positive than negative, and is thought to be a relatively stable dispositional trait (Scheier and Carver, 1985). Optimism could therefore be characterised with personality as a ‘personal resource’ which predisposes to well-being, but recent theories of flourishing have included optimism as an aspect of eudemonic well-being, or psychological functioning (Diener et al., 2010). According to the hypothetical model above, characteristics of the external environment, such as work characteristics, can influence well-being. Conversely, well-

being may shape perceptions of the environment. The relationships between well-being and job strain are investigated in Chapters 4 to 8.

#### **1.4 Positive psychological well-being and cardiovascular outcomes**

As outlined in the introduction, the possibility that happiness could promote longevity by protecting against heart disease has been widely reported in the national press. The evidence cited for these assertions typically comes from prospective epidemiological studies in which higher happiness at baseline is associated with a lower incidence of mortality or disease at follow-up. In the last decade a number of qualitative reviews (Pressman and Cohen, 2005; Veenhoven, 2008; Diener and Chan, 2011) and meta-analyses (Lyubomirsky et al., 2005a; Howell et al., 2007; Chida and Steptoe, 2008) have analysed the evidence from prospective studies linking baseline well-being and survival. All have concluded that positive well-being is associated with reduced mortality rates. The relationship between well-being and cardiovascular outcomes specifically has been the topic of a number of narrative reviews (Boehm and Kubzansky, 2012; Dubois et al., 2012; Lamers et al., 2012) and one meta-analysis (Chida and Steptoe, 2008). The meta-analysis by Chida and Steptoe (2008) identified a significant protective effect of well-being on mortality in healthy populations, combined hazard ratio, HR 0.71 (95% C.I. 0.72 to 0.98), based on 6 studies. The hazard ratio within patient cohorts was not statistically significant (HR 0.93, 95% C.I. 0.86 to 1.01), based on 5 studies. The authors suggested that outcomes within healthy populations may not generalise to patient populations since well-being may have distinct effects on disease onset and/or progression.

Methodological limitations of observational studies mean that a significant association between baseline well-being and later CVD does not necessarily indicate a causal explanation. Poor physical health at baseline could explain both low well-being and increased mortality to confound an apparently significant association. Higher quality studies therefore control for health status at baseline, preferably using objective medical records. Studies in healthy populations can exclude patients with known CVD and control for diagnosed disease but undiagnosed illness could still act as a confounder. Controlling for baseline disease severity in patient populations is complex and likely to require multiple clinical indicators. Studies with a longer follow-up or which exclude deaths occurring soon after baseline may help reduce the influence of undiagnosed terminal

declines on well-being and outcomes. Other potential confounders of the association between well-being and CVD include socio-economic status and behavioural risk factors such as diet, exercise, smoking and sleep quality, which have been linked to positive affect (section 1.3) and reduced CVD risk (NICE, 2010; Hoevenaar-Blom et al., 2011). Negative psychosocial factors such as hostility and depression could also confound an apparent association between well-being and CVD outcomes (section 1.1.2).

Other methodological issues to consider include the size and composition of the study cohort, since findings based on larger nationally representative samples are more likely to generalise to the wider population. Larger samples with longer follow-up and more events are more likely to have sufficient statistical power to detect small effects. The methods used to assess well-being and outcomes will also influence validity and reliability. Evidence of a specific association with cardiovascular outcomes is stronger for studies which use 'hard' outcomes such as stroke or MI which can be assessed by objective medical tests such as electrocardiograms, cardiac enzymes and angiography. Associations between well-being and 'soft' outcomes such as self-reported angina may be confounded by self-report biases, particularly when subjective well-being is also assessed using self-report metrics.

The most comprehensive review of studies examining the relationship between subjective well-being and cardiovascular outcomes to date was by Boehm and Kubzansky (2012). They found strong evidence of a relationship between well-being and reduced risks of CVD-related outcomes in healthy populations, based on 17 studies published up to 2011. There was an inconsistent association in 10 patient population studies. The evidence for reduced risks was strongest for optimism and vitality measures. (Vitality has been defined as active engagement with the world, and typically includes both measures of activated positive affect and sense of purpose)(Boehm et al., 2011a). The authors did not differentiate between experienced hedonic affect and more evaluative measures. The review also did not screen papers for methodological quality. It included some studies which did not statistically control for the effects of negative psychosocial factors.

### *Search strategy: well-being and cardiovascular outcomes*

I aimed to review higher quality prospective studies examining the association between subjective well-being and cardiovascular outcomes published from 1990 up to May 2013.<sup>8</sup> In addition to a keyword search, papers which cited the Boehm and Kubzansky (2012) review were searched for relevant studies. Criteria for inclusion were: prospective cohort design; full paper in English available; report of the association between positive psychological well-being and either a) clinically validated incident CVD/CHD outcomes in a population free of disease at baseline, or b) mortality/cardiac-related outcomes in a patient population controlled for measures of baseline disease severity. Unlike the review by Boehm and Kubzansky (2012), I included only studies which controlled for negative psychosocial risk factor(s) for CVD, to highlight distinct effects of positive well-being. Effect sizes were reported in fully adjusted models after controlling for conventional behavioural risk factor(s) for CVD, to reduce potential confounding. To limit the influence of un-diagnosed terminal diseases on short-term outcomes, studies needed to report at least 2 years follow-up in healthy populations and 6 months in patient populations. Details of study cohorts, measures, covariates, outcomes and strength of association in fully adjusted models were extracted and findings listed by well-being indicator: optimism, eudemonic well-being, hedonic well-being, evaluative well-being.

#### **1.4.1 CVD risk within in healthy populations**

Within healthy populations, 15 articles met the eligibility criteria based on 13 different cohorts. One study which examined self-reported stroke as an outcome did not strictly meet the criteria for a 'hard' clinical outcome, but the authors cited evidence based on the same cohort showing that self-reported stroke had high sensitivity and specificity (Kim et al., 2013b).

These 15 articles reported associations between 18 different subjective well-being constructs (n=5 optimism, n=5 eudemonic, n=5 hedonic, n=2 vitality, n=1 evaluative) with one or more cardiovascular outcomes. The relationships between each construct and CVD outcomes in healthy populations are listed in Table 1.3, in order of subjective well-being

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<sup>8</sup> Pubmed and PsycInfo keyword search terms: (prospective OR longitudinal) AND (well-being OR "positive affect" OR "positive emotion" OR "purpose in life" OR ikigai OR eudem\* OR optimis\* OR vitality) AND (cardiovascular OR heart)

measure. Of the 17 studies reviewed by Boehm and Kubzansky (2012), three were excluded: two studies did not control for negative psychosocial health (Martin et al., 2002; Giltay et al., 2004), one study had insufficient follow-up (Richman et al., 2009). The new study reported a significant association between purpose in life and reduced risk of incident stroke (Kim et al., 2013b). (An earlier article based on the same US cohort (Kim et al., 2011) was not included separately because the findings were duplicated by the 2013 paper, based on a longer follow-up.)

Overall, 12 out of the 18 well-being measures had a significant protective effect on one or more cardiovascular outcomes in fully adjusted models: 5/5 optimism, 3/5 eudemonic well-being, 2/5 positive affect, 1/2 emotional vitality, 1/1 life satisfaction. There was evidence that five out of six remaining well-being measures had protective effect in a specific subgroup (n=3 men only) or before adjustment for other psychosocial covariates (n=2). In terms of specific CVD outcomes, in fully adjusted models, one or more well-being measure significantly predicted incident CHD in 5/8 studies, stroke in 3/5 studies and CVD mortality in 5/7 studies. Only one study reported no significant associations between well-being and incident CHD (Nabi et al., 2008). Notably, no studies reported a significant association between well-being and increased disease risk.

In general study quality was high with the majority of associations assessed in large cohorts (n>5,000 in 8/13 cohorts) with a minimum four years follow-up. All studies were based in populations without CVD at baseline, with one exception which examined stroke outcomes and adjusted for baseline CVD (14% of the sample) (Ostir et al., 2001). All studies adjusted for smoking plus either BMI or other health behaviours, in addition to one or more measures of negative affect. All studies adjusted for baseline socio-economic status, with one exception (Davidson et al., 2010). Several studies also reported an association between well-being and CVD outcomes after adjusting for baseline blood pressure and metabolic indicators such as cholesterol, BMI and triglycerides (Giltay et al., 2006; Kubzansky and Thurston, 2007; Surtees et al., 2010; Boehm et al., 2011a; Kim et al., 2013b), implicating alternative explanatory pathways.

**Table 1.3 Optimism and CVD related end-points in healthy cohorts**

First author (Date)	Population (nation), follow-up	WB measure (time frame)	Negative emotion /stress covariates	Other covariates	Association with CVD outcome (fully adjusted model, 95% C.I.)
Kubzansky (2001)	1,306 men in community; age 50+, mean 60yr (USA), 10 Y	Optimistic explanatory style, 263-items	Anxiety or anger/hostility or depression	Ag, Ed, FH, BP, Chol, BMI, S, AI	(+) Highest tertile RR (adj dep) 0.63 (0.49-0.80) total incident CHD <i>(including angina, verified by physician)</i>
Giltay (2006)	313 older men; age 64-84, mean 71yr (Netherlands), 15 Y	Optimism, 4-items	Zung Self-rating Depression Scale	Ag, Ed, L, FH, SRH, D, Htmed, Chol, MAP, BMI, S, AI, PA	(+) Highest tertile, HR 0.51 (0.26-0.98) CVD mortality
Tindle (2009)	97,253 women, age 50-79yr, Women's Health Initiative (USA), 8 Y	Optimism, 6-item LOT-R	Depressive symptoms (& independent of cynical hostility)	Ag, Ed, In, Et, Ht, D, HRT, BMI, S, AI, PA	(+) Highest quartile, sig for incident CHD, HR 0.91 (0.83-0.99) and CVD mortality
Boehm (2011a)*	7,956 men & women; age 39-64, mean 50yr Whitehall II cohort (UK), 5Y	1. Optimism, 1-item 2. Emotional vitality, 5-items <i>(generally/ 4 weeks)</i>	Ill-being y/n (based on depression, anxiety; or stress)	Ag, Sx, Et, MS, Oc, D, Tri, Chol, BP, BMI, FV, AI, S, PA	1. Higher optimism (+) , +1SD, HR 0.87 (0.78-0.97) incident CHD <i>(fatal CHD, first MI, diagnosed angina)</i> 2. Higher vitality (+/-), +1SD, HR 0.89 (0.78-1.01) incident CHD, sig. before adjusting for ill-being <i>Separate models</i>
Kim (2013)*	6,739 men & women stroke-free; age >50, mean 69yr, Health and Retirement Survey (USA), 4 Y	1. Purpose in life (7-item) 2. Optimism (LOT-R) 3. Positive affect	Anxiety, cynical hostility, depression, negative affect, neuroticism, pessimism	Ag, Sx, Et, Ed, MS, SRH, Ht, D, HD, OCD, BP, BMI, AI, S, PA, social participation	1. Purpose in life (+) continuous OR 0.86 (0.74-1.00, p=0.049) self-report stroke incidence 2. Optimism (+) high vs low OR 0.87 (0.77-0.99) stroke incidence 3. Positive affect (+/-) not significant in <i>same model</i>

**Table 1.3 Eudemonic constructs and CVD related end-points in healthy cohorts**

First author (Date)	Population (nation), follow-up	WB measure (time frame)	Negative emotion /stress covariates	Other covariates	Association with CVD outcome (fully adjusted model, 95% C.I.)
Sone (2008)	43,391 men & women; age 40-79, mean 60y, Ohsaki region (Japan), 7Y	Ikigai = sense of purpose in daily life, single item	Perceived mental stress (high/ moderate/low)	Ag, Sx, Ed, MS, Oc, SRH, P, D, Ht, OCD, PF, BMI, S, Al, PA, SI	(+) none vs ikigai, HR sig for CVD mortality 1.6 (1.3-2.0)
Koizumi (2008)	1,618 men & women; age 40-74, mean 56yr, O-town region (Japan), 13 Y	Ikigai, single item	Perceived stress (high/low)	Ag, Occ, Ht, D, S, Al, PA	(+/-) High vs low, sig for stroke mortality in men only, not sig for CVD mortality e.g. men HR 0.56 (0.28-1.10) CVD mortality
Tanno (2009)	73,272 men & women; age 40-79, mean 56yr, Collaborative Cohort Study (Japan), 12 Y	Ikigai, single item	Perceived stress (high/moderate/ low)	Ag, MS, Oc, Ed, Ht, D, BMI, PA, S, SI	(+/-) Ikigai vs none, sig for CVD mortality in men only, not sig for CHD/stroke; e.g. men>5yrs f-up, HR 0.86 (0.76-0.97) CVD mortality
Surtees (2010)	19,067 men & women; age 41-80, mean?, EPIC-Norfolk study (England), 11 Y	Mastery, 7-item scale	Past year major depression, neuroticism, hostility, sense of coherence	Ag, Sx, Oc, Ad, D, Ht, BP, Chol, BMI, S, Al, PA	(+) Continuous score, SD decrease: HR 1.11 (1.00-1.23) CVD mortality - but not sig for men or women alone  (+) Purpose in life OR 0.86 (0.74-1.00) stroke incidence <i>self-report</i>
See also Kim (2013)**: Purpose in Life (in Optimism table above)					



**Table 1.3 Hedonic well-being and emotional vitality with CVD related end-points in healthy cohorts**

First author (Date)	Population (nation), follow-up	WB measure (time frame)	Negative emotion /stress covariates	Other covariates	Association with CVD outcome (fully adjusted model, 95% C.I.)
Ostir (2001)	2,478 men and women; age 65+yr, EPESE North Carolina Study (USA), 6 Y	Positive emotions from 4-item CESD ( <i>last week</i> )	Negative affect (16-item CES-D)	Ag, Sx, Ed, In, MS, MI, DBP, BMI, S	(+) Continuous score on 5-point scale, 0.74 (0.62-0.88) stroke incidence <i>based on physician diagnosis</i>
Nabi (2008)	8,918 men and women, age 39-64, Whitehall II cohort (UK), 12.5 Y	Positive affect, Bradburn affect balance scale ( <i>last few weeks</i> )	Psychosocial stress at work, negative affect	Ag, Sx, SES, Ht, Htmed, Chol, BMI, FV, S, Al, PA	(null) ns in adjusted or unadjusted models, highest tertile HR 1.04 (0.85 to 1.29) incident CHD <i>including cardiologist confirmed angina</i>
Shirai (2009)	88,175 men and women, age 40 to 69, Public Health Center-Based Cohort (Japan), 12 Y	Life enjoyment, single item	Perceived mental stress, type A personality (anger, hostility, competitive)	Ag, Oc, Ht, D, HS, BMI, S, Al, PA	(+/-) Lowest tertile enjoyment sig. for stroke/ incident CHD/ CVD mortality in men only e.g. men HR 1.61 (1.32-1.96) CVD mortality
Davidson (2010)	1,739 men and women; age 18+, mean 46y, Nova Scotia Health Survey (USA), 10Y	Trained nurses coded degree of outwardly displayed positive affect, rated 1-5	CES-D, Cook Medley Hostility Scale, Spielberger Trait Anxiety Inventory	Ag, Sx, D, Chol, BP, BMI, S	(+) Continuous score, HR 0.78 (0.63-0.96) incident CHD ( <i>physician diagnosed</i> )
<i>See also Kim (2013)**: Positive affect (in Optimism table above)</i>					(+/-) not sig. after adjustment for both purpose in life and optimism
Kubzansky (2007)	6,025 men & women; aged 25-74, mean 47, National Health and Nutrition Survey (USA), 15 Y	Emotional vitality, 6-items General Well-Being Schedule ( <i>last month</i> )	Psychological condition y/n, psychotropic medication y/n	Ag, Sx, Et, MS, D, Ht, BP, Chol, BMI, S, Al, PA	(+) Highest tertile, HR 0.81 (0.69-0.94) incident CHD
<i>See also Boehm (2011)**: Emotional vitality (in Optimism table above)</i>					(+/-) Highest tertile vitality, +1SD, HR 0.89 (0.78-1.01) incident CHD

**Table 1.3 Evaluative well-being constructs and CVD related end-points in healthy cohorts**

First author (Date)	Population (nation), follow-up	WB measure (time frame)	Negative emotion /stress covariates	Other covariates	Association with CVD outcome (fully adjusted model, 95% C.I.)
Boehm (2011b)	7,956 men & women; age 39-64, mean 50yr Whitehall II cohort (UK), 5Y	Life satisfaction in 8 domains	Ill-being y/n	Ag, Sx, Et, MS, Oc, D, Tri, Chol, BP, BMI, FV, Al, S, PA	(+) Continuous score, HR 0.74 (0.55- 0.99) total incident CHD, driven by angina. Sig. for separate job, family, sex life, self satisfaction domains.

HRS = Health and Retirement Survey, WII = Whitehall II cohort, LOT-R = Life Orientation Test Revised

\*first appearance of study in table (detailed), \*\*further listing of study in table (different outcome)

Covariates listed in order of sociodemographics (Ag=age, Sx=sex, Et=ethnicity/race, SES=socioeconomic status, Ed=education, In=income, MS=marital status, Oc=occupation/job), baseline health (SRH=self-rated health, FH=family history CHD, Ht=hypertension, Htmed=hypertensive medication, MI=history of infarction, D=diabetes, HRT=hormone replacement therapy, OCD=other chronic diseases, BP=blood pressure, MAP=mean arterial pressure, Chol=LDL/HDL/ cholesterol, Tri-triglycerides, BMI=body mass index), health behaviours (FV=fruit and vegetable consumption, Al=heavy alcohol consumption, S=smoking, PA=physical activity, Sl=sleep)

Two studies based on nationally representative samples in the USA both found significant associations with CVD outcomes: purpose in life and optimism predicted stroke incidence in older adults (Kim et al., 2013a) and emotional vitality predicted CHD in adults aged 25-74 years (Kubzansky and Thurston, 2007). Of the cohorts which were based on a representative sample of a specific geographic region, Surtees et al. (2010) found that mastery predicted CVD mortality in adults 41-80 in Norfolk (UK). In the USA, positive affect predicted stroke incidence in older adults (Ostir et al., 2001). Interviewer-ratings of positive affect predicted incident CHD over 10 years in adults aged 18 and above (Davidson et al., 2010). In Japan, ikigai (sense of purpose) was associated with increased mortality in a large representative sample of middle-aged adults in the Ohsaki region (Sone et al., 2008) but one smaller regional study and two larger multicentre studies only found significant associations in men: for ikigai and CVD mortality (Tanno et al., 2009), ikigai and stroke mortality (Koizumi et al., 2008) and life enjoyment with stroke, incident CHD and CVD mortality (Shirai et al., 2009).

Optimism was a significant predictor of CVD outcomes in all five studies. In addition, Kim et al. (2013b) demonstrated that optimism and purpose in life had independent associations with stroke incidence, whereas positive affect was not a significant predictor in the same study. There was a mixed pattern of associations for other dimensions of well-being with some statistically significant effects and other null associations. There did not appear to be clear differences in the consistency of significant effects by well-being metric, CVD outcome, cohort age or size, length of follow-up or covariates.

The only study which found no association between positive affect and incident CHD, regardless of covariates, was based on 12-year follow-up of the Whitehall II cohort (Nabi et al., 2008). The Whitehall II study was set up to examine the health of 10,300 working men and women aged 35 to 55 years in 1985, across all grades of the civil service, of whom two thirds were men (Marmot et al., 1991). The study by Nabi and colleagues included almost 9,000 adults and generated a large number of cases (>600) so lack of statistical power is unlikely to have accounted for the null results. Later analyses of the same cohort did find that CHD was predicted by optimism, emotional vitality (though not after adjustment for ill-being) and life satisfaction related to work, sex life, self and family (Boehm et al., 2011a; Boehm et al., 2011b).

Emotional vitality included items assessing energy and feeling 'full of life' so may be more likely to have been related to physical health than other well-being measures. The study was based on a broad sample of civil servants in London in 1985, and findings may not generalise to other occupations.

Interestingly, three large studies in different Japanese cohorts identified a significant association between well-being and stroke or CVD mortality in men, but not in women (Koizumi et al., 2008; Shirai et al., 2009; Tanno et al., 2009). The study by Koizumi was based in a relatively small ( $n < 1,700$ ) and comparatively young (mean age 56 years) cohort which may have had insufficient cases. The studies by Tanno and Shirai, however, each involved over 70,000 people over 12 years follow-up and controlled for multiple health behaviours and measures of negative psychosocial health. The fact that gender differences were not reported in studies based on US or European cohorts suggests that there could be socio-cultural gender differences in the expression of *ikigai* or life enjoyment in Japan, which are not present in Western cultures.

#### **1.4.2 CVD outcomes within patient populations**

Seven studies within patient populations met the inclusion criteria (Table 1.4). Six out of 10 studies included in the Boehm and Kubzansky (2012) review were excluded: four did not control for negative psychosocial health (Middleton and Byrd, 1996; Agewall et al., 1998; van Domburg et al., 2001; van der Vlugt et al., 2005); one was in non-cardiac patients (Einvik et al., 2009) and one had insufficient follow-up (Scheier et al., 1989). Five of the seven included studies reported an independent protective effect of subjective well-being on re-hospitalisation ( $n=2$ ), incident MI ( $n=1$ ), all-cause mortality ( $n=1$ ) or death/MI ( $n=1$ ) and two further studies found an association with mortality that was significant before adjustment for negative affect.

All studies in patient populations adjusted for baseline CV health to some extent, but control for other co-morbidities, sociodemographic factors and health behaviours was limited. For example, only one study adjusted for physical activity (Kim et al., 2013a), which has been shown to predict positive affect (Pasco et al., 2011) in addition to promoting recovery from cardiac injury (Giallauria et al., 2012). The study by Kim et al., (2013) was the only study

based on a nationally representative sample of cardiac patients. In this study, optimism and purpose in life predicted incident MI, independent of baseline disease severity (assessed with 7 objective indicators), anxiety, hostility and depression. Positive affect was not a significant predictor of acute MI in the same model. The two studies which did not find a significant independent protective effect of positive emotions on mortality were both relatively large studies with over 10 years follow-up up but neither study used a standardised measure of subjective well-being (Barefoot et al., 2000; Brummett et al., 2005). Two smaller studies which did report an independent effect of well-being also had methodological weaknesses: a study in 874 cardiac patients by Denollet et al. (2008) was limited to a two year follow-up and a study Birket-Smith et al. (2009) included only 85 patients. Two studies reported an association between optimism and a reduced likelihood of re-hospitalisation (Scheier et al., 1999; Tindle et al., 2012). Arguably this outcome is a less reliable indicator of disease progress than mortality or incident MI because individuals may be able to choose not to be re-hospitalised under some circumstances, such as if they have support at home.

**Table 1.4 Well-being and CVD related end-points in patient cohorts**

First author (Date)	Population (nation), follow-up	WB measure (time frame)	Negative emotion /stress covariates	Other covariates	Association with CVD outcome /mortality (fully adjusted model, 95% C.I.)
Scheier (1999)	309 male & female consecutive CABG patients, mean age 63y (USA), 6 mth	Optimism, LOT-R	Depression, neuroticism, pessimism	Ag, Sx, Ed, MS, Occ, Ht, D, chol, grafts, vessels, NYHA class, S	(+) Continuous score, OR 0.32 (0.12-0.96) CABG-related rehospitalisation
Tindle (2012)	430 male & female post-CABG patients, mean age 65y (284 depressed), 8 mth	Optimism, LOT-R	Depression, anxiety, mental quality of life	Ag, Ed, physical quality of life, social support, adherence, S, PA	(+) Upper quartile optimists less likely to be rehospitalised OR 0.54 (0.32-0.93)
Kim (2013)	1,546 men and women with CHD; age 53-101, mean 72yr, Health & Retirement Survey (USA), 2Y	1. Purpose in life (7-item) 2. Optimism (LOT-R) 3. Positive affect	Anxiety, cynical hostility, depression	Ag, Sx, Et, Ed, MS, CHD severity (combining 7 indicators), BP, S, PA, Al, BMI	(+) High vs Low optimism OR 0.68 (0.54-0.87) incident MI. (+) Purpose in life OR 0.76 (0.58-<1.00) incident MI ( <i>physician confirmed</i> ) (In the <i>same model</i> , PA not a sig.)
Barefoot (2000)	1250 male & female angiography patients, mean age 52y (USA), 15.2 Y	Positive affect (derived from Zung depression scale)	Negative affect from Zung sub-scale	Ag, Sx, In, MiD, EF, ECGab, vessels	(+/-) Continuous score, RR 1.26 for survival from cardiac death (p=0.001), but not sig. after adjustment for negative affect
Brummett (2005)	866 male & female angiography patients, mean age 60y, confirmed CAD (USA), 11.4 Y	Positive emotions, 8-item personality inventory	Zung Self-rating Depression Scale	Sx, HF, EF, vessels, S	(+/-) Continuous score, HR 0.88 (0.72-1.07) for all-cause mortality, sig. before adjustment for depression
Denollet (2008)	874 men undergoing stent implantation (Netherlands) 2 Y	Positive affect, 4-items from HADS	Negative affect, depression, anxiety	Ag, Sx, Ht, D, CABG surgery, Chol, vessels, renal impairment, stent type, S	(+) 1 SD increase in PA, HR 0.85 (0.78-0.92) for death or MI ( <i>physician confirmed</i> )
Birket-Smith (2009)	85 male and female cardiology outpatients, mean age 65y (Denmark), 6 Y	WHO-5 Well-being Index	Mental disorder	Ag, social contacts, cardiac diagnosis, somatic disease, OCD	(+) Binary variable, HR 0.98 (0.96-0.99) for all-cause mortality

Covariates as for Table 1.3 plus clinical diagnostics (MiD=myocardial damage, ECGab=electrocardiogram abnormalities, EF=ejection fraction, vessels=no. of vessels with >75% narrowing, grafts=no. of grafts. HADS=Hospital Anxiety and Depression Scale

### **1.4.3 Summary and limitations of the evidence from prospective studies**

The majority of studies in healthy populations found that higher subjective well-being was associated with a reduced risk of CVD, independent of baseline health, negative affect, demographic factors and health-related behaviours. Significant associations were found in a number of large-scale representative population cohorts in the USA and in the Whitehall II and EPIC-Norfolk UK cohorts. Associations were more consistent in men than in women in Japan, suggesting that there may be cultural gender differences. Seven out of seven studies in cardiac patients also reported a trend for an association between higher baseline well-being and reduced CVD morbidity or mortality, but only one study was based on a nationally representative sample.

Optimism was the most consistent predictor of reduced CVD risk in both healthy population samples and cardiac patients, reinforcing the findings of the review by Boehm and Kubzansky (2012). Optimism reflects a trait for positive outcome expectancies, so may tap into a more stable disposition to experience positive emotions and cognitions than hedonic or evaluative well-being measures. All of the studies which assessed self-reported positive affect used a general frame of reference or a time frame of a week or more, which could lead to errors in recollection, recall biases or salient memory heuristics (Miron-Shatz et al., 2009). These biases could be limited by using repeated measures of experienced affect; for example, Steptoe and Wardle (2011) found that happiness rated four times over the day predicted increased survival over five years in a representative sample of older English adults. Self-report biases were eliminated in the study by Davidson and colleagues (2010), in which trained interviewers rated the expression of positive emotions. Interestingly, optimism and purpose in life both had independent predictive effects for incident stroke and for acute MI in cardiac patients (Kim et al., 2013a; Kim et al., 2013b). These effects were not independent of positive affect, but optimism, purpose in life and positive affect were positively correlated. Other large-scale studies identified significant effects of vitality (Kubzansky and Thurston, 2007) and evaluative measures of well-being (Boehm et al., 2011b) on reduced CVD risk, supporting the proposal that these different measures could represent related dimensions of the same underlying construct of subjective well-being (section 1.2.4).

In this qualitative review I was unable to detect any clear patterns linking specific well-being indicators with specific disease endpoints, or linking study quality to outcomes. The heterogeneity of well-being indicators, covariates and outcomes also made it difficult to compare effect sizes between different studies. A quantitative review using meta-analytic techniques would enable further investigation of these issues. The earlier meta-analysis by Chida and Steptoe (2008) reported almost a 30% reduced risk of cardiovascular mortality associated with higher well-being (combined hazard ratio, HR 0.71, 95% C.I. 0.52 to 0.98) based on six healthy population studies. The effect in fully adjusted models is likely to be smaller, but several large-scale studies in the current review reported that well-being was independently associated with more than a 20% reduced risk of incident CHD (based on a  $HR < 0.80$ ) (Kubzansky et al., 2001; Davidson et al., 2010; Boehm et al., 2011b). A further advantage of using meta-analytic techniques would be to investigate publication bias. Studies that report null findings are less likely to be published than are studies that detect an association, which could lead to an overestimation of effects (Rosenthal, 1991).

It remains unclear from the observational studies in this review whether the absence of positive well-being is a direct cause of CVD. Reverse causality is unlikely to have accounted for associations in healthy populations with extended follow-up and multiple controls for objective and self-reported baseline health, e.g. (Kubzansky and Thurston, 2007; Boehm et al., 2011a; Kim et al., 2013b). Baseline diabetes, blood pressure, cholesterol and lipids did not account for the association between well-being and outcomes. The majority of studies reported protective effects on CVD outcomes after adjustment for multiple measures of negative mood and personality. Environmental exposures such as work stress have received little attention in observational studies to date, so there may have been unmeasured influences of exposure to stress. Disentangling independent effects of baseline health, positive and negative affect on cardiac outcomes in patients with atherosclerotic disease is problematic, because circulating pro-inflammatory cytokines which are associated with worse cardiovascular prognosis (Wannamethee et al., 2009) may also induce low mood (Wright et al., 2005). Most studies in patient populations adjusted for few behavioural and psychosocial factors, probably because of the difficulties of recruiting large representative patient populations, so the evidence of a distinct effect of psychosocial well-being is less strong. Healthy population studies all adjusted for health-related behaviours at baseline but well-being may predict future health-protective behaviours which were unaccounted for (Petroczi



et al., 2010). Future studies with repeated measures of well-being, behavioural and negative psychosocial covariates over time are needed to investigate the dynamic associations between changes in well-being and cardiovascular outcomes.

Subjective well-being could represent a marker of underlying protective biological, behavioural or temperamental factors, rather than a direct protective factor. For example, a common genetic substrate might account for the association between well-being and CVD risk. One study based on almost 4,000 Danish twin pairs over 70 years of age found that subjective well-being (based on positive affect and life satisfaction) predicted survival independently of familial factors of genes and shared environment, supporting a causal influence on mortality (Sadler et al., 2011). However, the Danish study did not account for health behaviours.

In summary, the papers in this review suggest that a causal association between subjective well-being and cardiovascular disease incidence and progression is possible, but has not been proven. The case for causality would be strengthened by evidence of plausible biological mechanisms through which subjective well-being could influence disease processes. These mechanisms will be investigated in Chapter 2. Interventions which promote well-being and subsequently reduce CVD risk would provide strong support for a causality argument; this topic will be reviewed in detail in Chapter 7.

## **Chapter 2 Psychobiological mechanisms linking well-being and cardiovascular disease processes**

In this chapter I review the evidence for direct influences of psychological well-being on biological processes relevant to cardiovascular disease. Section 2.1 introduces the pathways through which psychosocial factors are thought to influence atherosclerotic processes and provides a theoretical overview of the role for well-being. Section 2.2 outlines the empirical evidence linking well-being to biological markers, independently of negative psychosocial factors. I concentrate on reviewing in detail the evidence linking well-being with cardiovascular function and neuroendocrine activation since these systems will be investigated further in later chapters.

### **2.1 Psychosocial influences on biological processes implicated in CVD**

#### **2.1.1 An overview of the stress response system**

Organisms respond to constant changes in environmental conditions using continuous sensory monitoring and feedback systems co-ordinated by the brain. This dynamic 'steady state' is termed allostasis (Sterling and Eyer, 1988). Physical or perceived threats to allostasis activate the 'fight or flight' acute stress response, characterised by activation of the sympathetic branch of the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. The acute effects on the cardiovascular system arising from recognition of a threat are illustrated in Figure 2.1.

Sympathetic activation results in an increased heart rate and force of contraction, pro-inflammatory cytokine release, platelet aggregation and vasoconstriction in response to release of catecholamines. Cortisol, the end effector of the HPA axis, promotes the breakdown of carbohydrate to glucose, inhibits acute inflammation and works with the sympathetic system to increase blood pressure. These changes are adaptive in preparing the body for action and limiting the effects of physical injury. However, repeated and prolonged activation of the stress cascade, for example in response to a chronic environmental stressor, results in heightened circulation of stress mediators. This exposure is thought to exert physiological

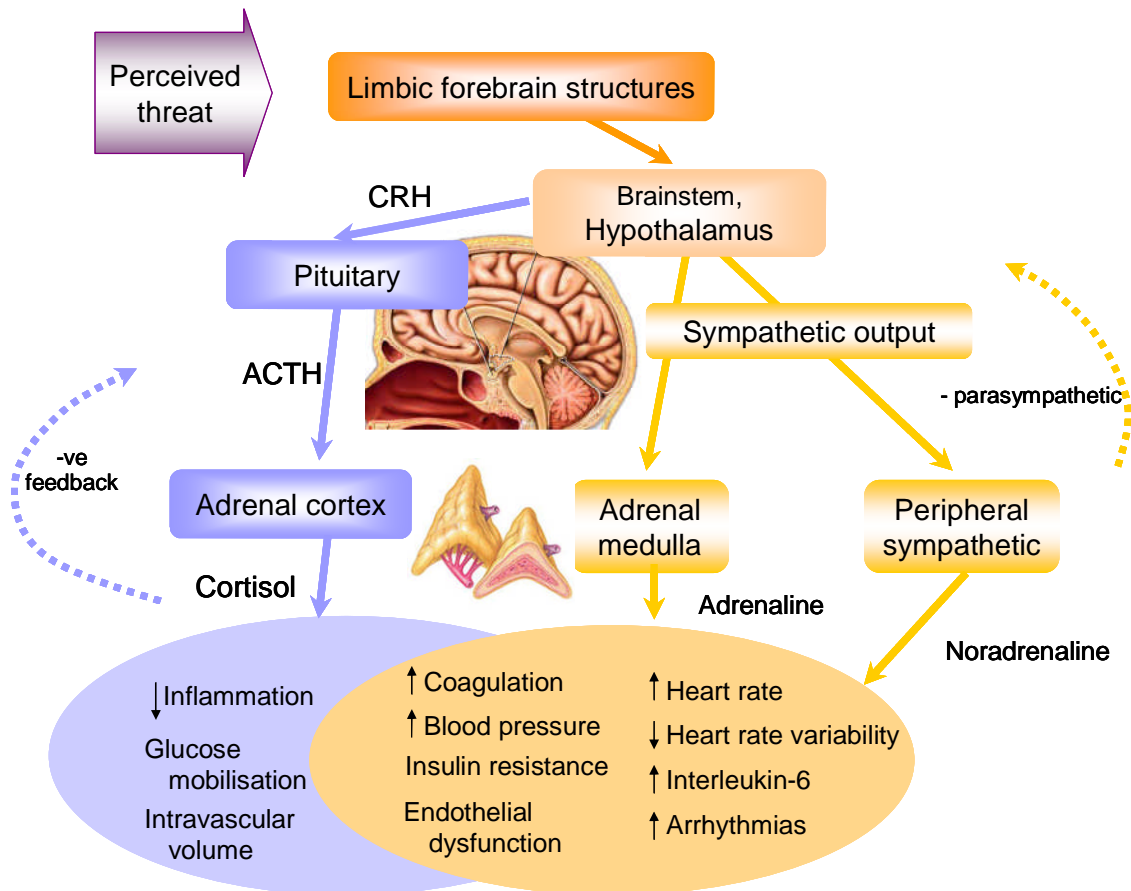
costs on the organism, termed 'allostatic load', increasing vulnerability to disease (McEwen, 2008). For example, chronically elevated cortisol is thought to promote insulin resistance, central adiposity and increase the risk of hypertension (Whitworth et al., 2005).

Individuals differ in their biological reactivity to stress. The magnitude of response and the ability to recover efficiently are thought to be determined by genetic factors, early life experience, perceptions of a specific stressor and coping resources (Lovallo, 2005). Whether or not psychosocial stress promotes CVD for a particular individual will therefore depend on both their intrinsic stress responsivity and their exposure to stress in daily life, in addition to other cardiovascular risk factors (Steptoe and Kivimaki, 2012; Steptoe and Kivimäki, 2013).

#### *Stress and atherosclerosis (the process underlying cardiovascular disease)*

Chronic activation of the stress response may promote atherosclerosis due to the increased shear stress associated with increased blood pressure, heightened circulating lipids, pro-inflammatory cytokines, platelet aggregation and/or endothelial dysfunction (Brotman et al., 2007). Atherosclerosis occurs when damage and inflammation of endothelial cells lining the vessel walls enables the penetration of white blood cells into the intima layer of smooth muscle. Macrophages engulf lipid particles which are deposited in the intima when the cells are oxidised forming 'fatty streaks'. Cycles of inflammation and lipid accumulation occur, gradually forming an atherosclerotic 'plaque' with a fibrous surface, narrowing the vessel lumen. Although reduced flow may cause symptoms such as angina, cardiovascular events usually occur as a result of rupture of the fibrous cap leading to clot formation, complete occlusion of blood flow and rapid death (infarction) to the tissues supplied by the artery (Galkina and Ley, 2009).

**Figure 2.1 Cardiovascular effects of the acute stress response**  
Focusing on activation of the hypothalamic-pituitary-adrenal axis (purple) and the sympathetic nervous system (yellow), adapted from (Brotman et al., 2007)



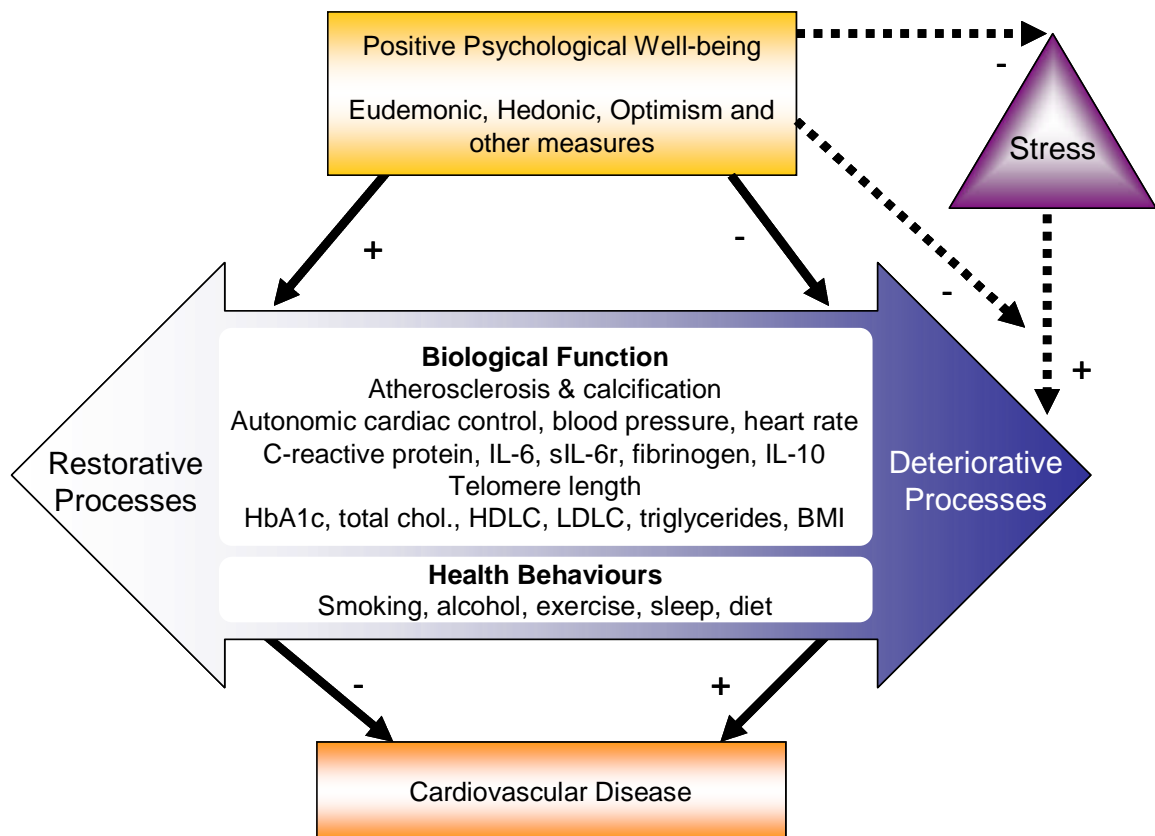
Activation of the sympathetic nervous system stimulates increased secretion of adrenaline and noradrenaline into the circulation. These hormones drive an increase in heart rate, force of contraction, peripheral vasoconstriction and mobilisation of energy reserves. The effects are limited by reflex activation of the opposing parasympathetic nervous system.

For the HPA axis, neurons in the paraventricular nucleus of the hypothalamus secrete corticotrophin-releasing hormone (CRH) into the portal circulation. This stimulates the anterior pituitary to secrete adrenocorticotrophic hormone (ACTH) which acts on the zona fasciculata of the adrenal cortex to stimulate synthesis and release of cortisol. Cortisol potentiates the effects of the sympathetic system on blood pressure and energy mobilisation.

### 2.1.2 How might well-being exert protective biological effects?

I proposed in Chapter 1 that positive well-being is not equivalent to the absence of psychosocial stress and that well-being has a distinct association with CVD risk. If this is the case, we would expect that well-being has biological consequences which are distinct from a simple absence of stress activation. In their recent review of the relationship between positive well-being and cardiovascular disease, Boehm and Kubzansky (2012) proposed that the association is mediated by both the presence of restorative processes and the absence of deteriorative processes (Figure 2.2). This model highlights the evidence that well-being is associated with the likelihood of engaging in restorative behaviours, such as sleeping for eight hours each night (versus short or prolonged sleep), in addition to lower rates of deteriorative behaviours such as smoking.

**Figure 2.2 Model of positive psychological well-being and cardiovascular disease**  
Adapted from Boehm and Kubzansky (2012). The authors noted that non-linear relationships are not explicitly depicted and that the direction of arrows does not imply that bidirectional pathways do not exist.



Most biological markers are treated on a continuum from low to high risk (for example C-reactive protein), so it may be difficult to demonstrate an association between well-being and 'restorative' levels which is independent from the absence of deteriorative processes (i.e. low levels). The authors suggest that future research will enable greater discrimination of biomarkers reflecting restorative cardiovascular processes.

Figure 2.2 also highlights the role of stress. The dotted lines suggest that well-being could either directly reduce levels of experienced stress and/or could buffer the effects of stress, but the authors do not discuss evidence for these pathways in detail. Well-being might exert its effects at the highest levels of the stress cascade by influencing the conscious evaluation of stimuli as threatening or benign. Lazarus hypothesised that positive emotions may help to prevent negative emotions under stressful conditions via appraisal of situations as a challenge rather than a threat (Lazarus, 1991). In an update to the transactional theory of stress and coping by Lazarus and Folkman (1984), Folkman (1997) demonstrated that positive and negative emotions co-occur in the context of chronic stress. A more recent review proposed roles for positive emotions in favourable psychological appraisals of the stressor and one's coping resources, in addition to promoting meaning-focused coping, which might involve actions to reduce the likelihood of further stress (Folkman, 2008).

In terms of neural evidence for differential conscious processing of threats associated with well-being, there is some evidence from neural imaging studies suggesting that positive emotional states and traits are associated with asymmetrical patterns of prefrontal cortex activation, part of the limbic circuitry governing emotional experience (Davidson, 2004). Left-sided prefrontal activation was also associated with psychological well-being in older adults (Urry et al., 2004). Left-sided activation of the prefrontal cortex in monkeys was also associated with low cortisol and CRH levels in monkeys (Kalin et al., 1998 ; Kalin et al., 2000), but this evidence does not appear to have been duplicated in humans.

It is possible that psychological well-being could be associated with reduced arousal of biological systems below the level of conscious processing, such as at the brainstem or hypothalamus, or even at a peripheral level. Alternatively positive affect might be associated with improved sensitivity of negative feedback mechanisms, enabling efficient termination

of the stress response. Rozansky and Kubzansky (2005) theorised that psychological well-being represented flexibility to emotionally respond to and recover from environmental challenges which was also reflected in physiological adaptability and avoidance of the chronic hyper-arousal associated with emotional disorders and chronic stress.

*Focus of this thesis: blood pressure and cortisol*

Evidence of psychobiological pathways underlying the association between psychological well-being and CVD has been reviewed in several recent papers (Pressman and Cohen, 2005; Steptoe et al., 2009; Dockray and Steptoe, 2010; Boehm and Kubzansky, 2012). A list of the biological markers implicated in the most recent review is included in Figure 2.2. These fall under the broad headings of atherosclerosis, cardiovascular function, inflammation, endothelial function, metabolic function and telomere length. Much of the evidence relates to markers of cardiovascular function, such as blood pressure, which are powerful indicators of future cardiovascular risk. Studies assessing cortisol were excluded from the most recent review because the authors felt that the link with CVD risk was unclear (Boehm and Kubzansky, 2012). Subsequent research has strengthened the associations between acute cortisol reactivity and the steepness of the diurnal slope with CVD outcomes (Kumari et al., 2011; Hamer et al., 2012). I therefore review the evidence linking well-being with cardiovascular function and cortisol. These associations will be explored further in later chapters of this thesis. The aim of the review is to identify gaps and inconsistencies in the literature to guide further research. In order to manage the scope of the review, evidence relating well-being to other biomarkers is summarised more briefly.

## **2.2 Studies investigating the biological effects of well-being**

### **2.2.1 Methods for investigating psychobiological mechanisms**

The mechanisms linking well-being and biological systems have been investigated using a range of methods including analyses of biomarkers in cross-sectional population studies, ambulatory monitoring studies and laboratory-based psychophysiological stress testing and mood induction studies. Many large cohort studies have started to collect biological data but to date most published studies which have examined associations with well-being have reported cross-sectional associations between questionnaire measures of subjective well-

being and single clinic-based assessments of biomarkers. For example, cross-sectional analyses of the Midlife in the United States (MIDUS) study identified cross-sectional associations between optimism and increased antioxidants (carotenoids), high-density lipoprotein (HDL) cholesterol and lower triglycerides (Boehm et al., 2013a; b). Although these studies have the advantage that results may generalise to the wider population, cross-sectional studies cannot provide evidence of dynamic associations.

Ambulatory studies involve repeated or continuous measures of cardiovascular activity or cortisol (via saliva samples) in an ecologically valid setting, often in combination with mood diaries. Intensive ambulatory studies with multiple measures per day over several days can generate large amounts of data and are usually conducted in smaller populations because of the expense and practical challenges of administration. Monitoring studies can be used for analyses of both within-person and between-person variation of the associations between affect and biology using multi-level modelling techniques. This can help to discriminate between associations with transient or 'state' emotions and dispositional or 'trait' measures. Participants in naturalistic studies may however be differentially exposed to daily stressors, which increases the complexity of between-person comparisons (Smyth et al., 1998).

Psychophysiological stress testing allows individual differences in responses to standardised behavioural challenges to be measured under controlled conditions and related to psychosocial factors (Chida and Hamer, 2008). The extent to which acute stress responses predict clinical outcomes is likely to depend on exposures during everyday life. In a meta-analysis of longitudinal studies, both raised blood pressure reactivity and delayed recovery predicted poor cardiovascular risk status at follow-up, with the most consistent associations reported for future systolic and diastolic blood pressure (Chida and Steptoe, 2010). Heightened cortisol reactivity has been shown to predict hypertension and progression of coronary artery calcification over three years (Hamer et al., 2012; Hamer and Steptoe, 2012). Laboratory mood induction studies have attempted to induce positive or negative moods using film clips or music to assess real-time changes in biological factors but the prognostic significance of such studies is unclear (Fredrickson et al., 2000).



### 2.2.2 Cardiovascular function and positive psychological well-being

*Markers of cardiovascular function: heart rate variability, blood pressure and heart rate*

Blood pressure (BP) is one of the most important risk factors for CVD (Chobanian et al., 2003). In the long-term, blood pressure is influenced by a wide range of genetic and behavioural factors but moment-to-moment changes are controlled by cardiac output and systemic vascular resistance. Sympathetic autonomic activation stimulates the heart and constricts blood vessels resulting in a rise in arterial pressure, which can be reinforced by cortisol release (Figure 2.1). Blood pressure varies significantly over the day and night so continuous 24-hour ambulatory blood pressure readings (ABP) are preferable to clinic measures (Mallion et al., 1999). Ambulatory and home BP readings also reduce the so-called 'white coat effect', a transient elevation in blood pressure associated with observation during measurement, which is not reliably associated with CVD. Home and ABP measures are more reliable predictors of cardiovascular outcomes than clinic measures (Sheikh et al., 2011). Negative emotional experiences are associated with transient elevations in blood pressure and heart rate (Kamarck et al., 2005). A systematic review which reviewed evidence from 14 cohort studies and four case-control studies also reported that exposure to chronic stress predicted future hypertension (Sparrenberger et al., 2009). None of the studies in the review by Sparrenberger and colleagues adjusted for measures of positive psychological well-being.

The degree of sympathetic versus parasympathetic autonomic innervation of the heart, also termed sympathovagal balance, is indexed by heart rate variability (HRV) (Thayer and Lane, 2007). Higher vagal tone and lower sympathetic activation raises the threshold for cardiac dysfunction and is associated with reduced risk of CHD mortality (Thayer and Lane, 2007). HRV can be assessed in the time and frequency domains. Under resting conditions HRV in the time domain mainly reflects respiratory sinus arrhythmia (RSA), the degree of respiration-linked variability in the heart rate. RSA is thought to be an index of cardiac vagal tone. Higher resting RSA is associated with greater parasympathetic activation and a reduced risk of future hypertension (Masi et al., 2007). Power spectral analysis of the frequency domain can be used to quantify low frequency (LF) and high frequency (HF) power. HF power is interpreted similarly to RSA. LF power has been interpreted in some studies as a measure of sympathetic activation, but recent studies suggest that LF power is related to baroreflex function (Goldstein et al., 2011). Resting heart rate is also an indicator of autonomic balance.

Low resting levels are associated with a low risk of cardiac mortality (Williams and Merhige, 2012). Both chronic psychosocial stressors, such as work stress, and momentary 'worry' have been linked to increased HRV and HR (Pieper et al., 2010; Clays et al., 2011).

Cardiovascular function can also be measured in the laboratory in response to standardised stressors. A meta-analysis of 36 studies published up to 2009 reported that cardiovascular reactivity predicted incident hypertension and delayed post-stress recovery was associated with progression of carotid intima-media thickness (Chida and Steptoe, 2010). A meta-analysis of over 160 articles studying reactions to laboratory induced stress in healthy populations found evidence that hostility and aggression predicted exaggerated cardiovascular reactivity whereas anxiety and negative affect were linked to hypo-reactivity. General life stress and negative affect predicted poorer cardiovascular recovery (Chida and Hamer, 2008).

#### *Review of studies assessing associations between well-being and cardiovascular function*

Studies which have reported associations between subjective well-being and cardiovascular function are summarised below and in Tables 2.1 and 2.2, ordered by methodology.<sup>9</sup> Only studies which reported associations between cardiovascular markers and positive affect after adjustment for one or more negative psychosocial factors were included in this review.

##### *a) Subjective well-being and daily cardiovascular function in monitoring studies*

Seven studies in healthy populations and two studies in patient populations were retrieved. Evidence was mixed; 4/7 studies in healthy populations and 1/2 patient population study found some evidence of an independent association between positive emotional characteristics and low ambulatory cardiovascular arousal.

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<sup>9</sup> A keyword search in Pubmed and PsycInfo was conducted for empirical studies which measured the association between subjective well-being and cardiovascular function (HRV, HR, BP). Studies were also identified by hand-searching the bibliographies of previous reviews (Pressman and Cohen 2005, Steptoe et al., 2009, Dockray et al., 2010, Boehm and Kubzansky 2012) and papers citing those reviews. Only studies for which full articles in English were available online were included.

**Table 2.1 Ambulatory/monitoring studies examining the association between well-being and cardiovascular function**

First author (Date)	Population (nation)	Study design	WB measure	CV measure	Negative emotion / stress covariate	Other covariates	Main finding (Green=sig. PA & CV association; orange=no association; yellow=partial/weak link with CV activation)
<b>Ambulatory/ daily CV function - healthy populations</b>							
Raikkonen (1999)	100 normotensive adults, mean age 36 yrs (USA)	24-hr ABP and mood assessed on 2 work, 1 rest day. Associations tested with baseline physiological and psychological measures.	Trait optimism & pessimism (LOT), PA & NA (EMA) based on ratings of 17 emotions experienced over 3 days	3 days x 24- hr ABP	NA, boredom, trait pessimism & anxiety	Sx, Occ, interpersonal social connections, exercise, posture, location, alcohol,	Within person, state PA & NA associated with higher BP. Optimism predicted low DBP (independent of pessimism) but anxiety and pessimism stronger predictors of SBP. <i>Trait optimism assd with higher PA over the day &amp; lower NA (but not independent of anxiety or pessimism).</i>
Ong & Allaire (2005)	33 mf normotensive older adults age 60+yrs (USA)	60 day diary for mood and BP, am and pm. Multilevel modelling applied to explore within- and between- person associations.	Trait (mean) and daily PA assessed with PANAS	60 days x self- assessed BP am & pm	NA (PANAS)	Social connectedness ( <i>was associated with higher PA</i> )	Trait PA assd with low SBP, NA with high SBP & DBP. Daily PA and social connectedness moderated the relationship between daily NA and BP - PA 'undid' NA-BP association, even after adjusting for trait measures.
Steptoe (2005)	216 healthy working adults aged 47 yr+, Whitehall II cohort (UK)	Association between mean ABP over 1 work day/evening and mean happy ratings over the day.	EMA happy rated 1-5 at each BP inflation (PA), % ratings 4/5 counted	1 x daytime ABP, HR	Psychological distress (GHQ30)	Ag, Occ, BMI, PhysAct, Sm	No association between PA (EMA) and BP. In men only, PA (EMA) associated with lower mean HR.
Steptoe & Wardle (2005) ( <i>follow-up to Steptoe et al. 2005, above</i> )	Longitudinal: 162 adults from 216 above followed up after 3 years	Association between mean ABP over 1 work day/evening and mean happy ratings over the day.	EMA happy rated 1-5 at each BP inflation (PA), % ratings 4/5 counted	1 x daytime ABP, HR	Psychological distress (GHQ30)	Ag, Occ, BMI, PhysAct, Sm	After 3 years, PA (EMA) quintiles still predicted mean HR in men. New cross-sectional effect of PA with lower ambulatory SBP.

**Table 2.1 Ambulatory/monitoring studies examining the association between well-being and cardiovascular function (continued)**

First author (Date)	Population (nation)	Study design	WB measure	CV measure	NA/ stress covariate	Other covariates	Main finding
<b>Ambulatory/ daily CV function - Healthy populations (continued) &amp; patient populations</b>							
Shapiro (2001)	171 female healthy nurses, mean age 38 yrs (USA)	24-hr ABP and mood rated over 4 days. Multilevel modelling applied for repeated measures.	EMA happy rated 1-5 at each BP inflation	4 days x 24-hr ABP, HR	Negative mood pairings with stressed, tired, anxious, angry	None	Little change in BP or HR observed for the intensity of happy (graded increases in BP and HR shown with higher ratings of negative moods, decrease with tiredness).
Raikkonen (2008)	201 healthy adolescents 14-16yrs (USA)	Association between ABP day & night with trait measures of optimism and pessimism, adjusting for state mood.	Optimism (LOT-R), state PA (EMA) (interested/involved/pleasant interaction)	2 x day ABP, 1 x night	Pessimism, trait anger, anxiety, EMA mood (positive and negative)	Sx, Et, BMI, posture, location, food, time of day, caffeine, Sm	No independent association between optimism and ABP day or night. Pessimism significantly associated with higher BP after adjustment for all covariates. PA positively associated with DBP.
Daly (2010)	186 younger adults (Ireland)	Association between ambulatory HR and mood assessed with DRM. Multilevel modelling applied for repeated measures.	PA & NA (EMA) based on mean ratings of 11 emotions over 20min-2hr intervals (DRM)	1 x daytime ambulatory HR	NA, personality, psychological distress	Ag, Sx, location, social interaction, activity, BMI, body fat, alcohol, Sm	NA - but not PA (EMA) - on the day associated with higher HR after adjustment for all within/between person covariates. Ambulatory (not resting) HR also predicted by psychological distress. Tiredness associated with lower HR.
Bhattacharya (2008)	76 patients with suspected CAD (UK)	Associations between 24hr ambulatory ECG, mean mood assessed with DRM & baseline depression assessed with regression.	Happy ratings via DRM	1 x 24hr ECG for day & night HRV	Depression (BDI)	Ag, Sx, CAD status, medication, BMI, Sm, PhysAct	PA associated with higher HF power during day (borderline at night), lower LF power day & night. (Patients with CAD with more depressed affect had greater LF & lower HF power).
Bacon (2004)	135 patients with CAD (USA)	48hr ambulatory ECG and mood diaries every 20 min while awake; within-person associations explored.	EMA PA=relaxed, happy NA=anger, stressed, sadness, tired	2 days x 24hr ECG for HF and LF HRV	NA	Posture, medication use, age, day of assessment	PA predicted higher LF power; NA associated with lower HF & lower LF power.

The longest monitoring protocol, described by Ong and Allaire (2005), involved morning and evening measurements of BP and affect based on the PANAS for 60 days in 33 healthy older adults. Trait positive affect, a general measure assessed before the monitoring protocol began, was associated with lower mean diastolic BP while negative affect was associated with higher mean systolic BP. Daily positive emotions were associated with diminished BP reactivity to negative emotions on the same day. The largest ambulatory monitoring study in older adults involved over 200 middle-aged adults from the Whitehall II cohort (Stephoe et al., 2005). Aggregated ratings of happiness measured 33 times over the day were not initially associated with ambulatory BP but were associated with a lower heart rate over the day in men. Three years later, the heart rate effect in men was replicated and an inverse association between happiness ratings and ambulatory systolic BP became apparent in men and women (Stephoe and Wardle, 2005). It is not clear why heart rate effects differed by gender, but it is possible that women engaged in greater interpersonal interaction during measurements, which has been associated with both positive affect and heightened cardiovascular reactivity (Warner and Strowman, 1995).

One study in 100 working adults also identified an association between optimism, a trait measure, and lower diastolic BP over three days (Raikkonen et al., 1999). This association was independent of moods rated on the day and pessimism. In contrast, a later study from the same group found no association between optimism and BP in over 200 healthy adolescents monitored over two school days (Raikkonen and Matthews, 2008). Pessimism was a stronger predictor of systolic BP. The authors questioned the psychometric properties of the optimism scale of the LOT-R in adolescents because it had low internal consistency. Two other studies, one in young adults and another in nurses, also found no association between aggregated measures of positive emotions over the day and ambulatory heart rate (Daly et al., 2010) or blood pressure (Shapiro et al., 2001). Both studies found an independent association between negative emotional characteristics and elevated ambulatory cardiovascular measures. The study by Daly and colleagues adjusted for several potential confounding influences including physical activity and social interaction.

Two studies reported that higher state positive affect was associated with higher BP (Raikkonen et al., 1999; Raikkonen and Matthews, 2008). It is possible that highly activated

positive states such as elation, according to the circumplex model (Russell, 1980), activate the cardiovascular system. Positive affect is also associated with high levels of physical activity (Poole et al., 2011), which could confound associations with cardiovascular activation in ambulatory studies, but these studies both accounted for posture at the time of measurement.

In suspected CHD patients, positive affect over the day assessed retrospectively using the DRM was associated with greater HF HRV assessed with a 24-hour ECG (Bhattacharyya et al., 2008). In contrast, a larger study of CHD patients found that negative affect was associated with both HF and LF HRV, whereas positive affect had a positive association with LF HRV (Bacon et al., 2004). This study involved affect ratings every 20 minutes during waking hours and it is possible that this intensive protocol may have led to atypical ratings.

*b) Subjective well-being and CV measures in laboratory studies*

Four studies which assessed the influence of both positive and negative emotional characteristics on task reactivity or recovery to standardised mental stress tasks were identified, plus two studies which used a mood induction protocol and one study which used a negative emotional recall task (Table 2.2).

In 3/4 psychophysiological stress studies which applied mental stress tasks, positive emotions predicted faster diastolic BP recovery. The specific association depended on the measure of positive emotion. In 72 young men, our group found that EMA ratings of happiness measured over two days predicted lower systolic BP and faster diastolic BP recovery to mental stress tasks, after controlling for negative affect and effort reward imbalance, a measure of chronic work stress (Steptoe et al., 2007a). A retrospective measure of positive affect, based on PANAS responses over the last week, was not associated with BP recovery. In students faced with a mock examination task, trait positive affect but not state measures predicted more efficient recovery of low to high frequency HRV (Papousek et al., 2010). In the same study, state joy predicted less efficient HRV recovery. These studies suggest that there may be a distinction between state and trait or experienced measures of positive affect in associations with cardiovascular function. In a study involving 56 students, Dowd et al. (2010) found that baseline PANAS positive affect was associated with increased systolic BP reactivity to a stressful task, but also faster BP recovery to both a speech task and a control reading task.

**Table 2.2 Laboratory studies examining the association between well-being and cardiovascular function**

First author (Date)	Population (nation)	Study design	WB measure	CV measure	NA/ stress covariate	Other covariates	Main finding
<b>Laboratory stress reactivity and recovery</b>							
Papousek (2010)	65 healthy students (Austria)	Tested associations between trait and state PA & NA before during and after exam-style mental stress test.	Trait PA using PANAS and state joy rating	HR, LF/HF HRV, BP reactivity & recovery	Adjusted for trait NA or state anxiety and stress	baseline levels of each variable	Higher trait PA predicted faster DBP and HRV recovery, independent of NA. State joy predicted less efficient HRV recovery.
Stephoe (2007)	72 healthy young men, mean age 33yrs (UK)	Association between PA (PANAS) and CV responses to speech & mirror tracing tasks, tested on 2 occasions, 4 weeks apart.	EMA happy rating 4 times*2 work days (1-5), PANAS at lab session, past week	BP, HR reactivity & recovery	NA (PANAS), work stress (ERI)	Ag, BMI	PA (EMA) & PA (PANAS) associated with lower SBP at baseline and during stress test; no association with reactivity or recovery. PA (EMA), not PANAS, associated with lower baseline DBP and faster post-stress DBP recovery. No association with HR.
Brummett (2009)	328 healthy adults (USA)	Association between general PA and CV reactivity/recovery during anger recall and sadness recall tasks.	General PA based on factor analysis of 3 scales, assessed before, during & after tasks	BP, HR reactivity & recovery	General NA	Ag, Sx, In, Et, BMI, Sm	General PA associated with lower SBP & DBP reactivity to sadness recall task, not anger recall. No association with HR. Higher PA associated between PA and HR. PA <i>also associated with lower mean noradrenaline concentration.</i>
Dowd (2010)	56 healthy female students (USA)	Participants randomised to speech task or silent reading control. Association between state PA and NA relation to BP over time assessed.	Current PA (PANAS)	BP reactivity & recovery	NA (PANAS)	Sm	Speech task induced higher NA and small effect on lower PA. Higher pre-task state PA predicted higher speech task SBP reactivity; higher PA & NA during the task both associated with faster post-task recovery. For control task, higher baseline PA asssd with lower DBP reactivity & faster recovery.
Stephoe (2005)**	216 healthy working adults aged 47 yr+ (UK)	Association tested between PA (EMA) and reactivity and recovery to mirror and stroop tasks.	EMA happy rated 1-5 at each BP inflation (PA), % ratings 4/5 counted	BP, HR reactivity & recovery	Psychological distress (GHQ- 30)	Ag, Occ, BMI, PhysAct, Sm	No difference in subjective stress, BP or HR responses to tasks by happiness quintile. <i>Happiness predicted lower fibrinogen response to stress.</i>

**Table 2.2 Laboratory studies examining the association between well-being and cardiovascular function (continued)**

First author (Date)	Population (nation)	Study design	WB measure	CV measure	NA/ stress covariate	Other covariates	Main finding
<b>Mood induction</b>							
Oveis (2009)	80 healthy students (USA)	RSA assessed in lab at rest & in response to PA- inducing images. WB assessed 1 and 8 months later.	Trait measures: personality, optimism, PANAS over the last month State measure: current PANAS	Resting RSA & response to +ve/-ve films	Yes - optimism adjusted for pessimism, PA for NA, extraversion for neuroticism	None	Trait measures of PA/optimism asssd with higher resting RSA independent of NA. No association between induced state PA or NA and RSA.
Radstaak (2011)	103 healthy students (USA)	Mood induction study. Examined associations between state PA, NA and rumination after mental stress task on CV recovery, using a +ve/- ve/control affect manipulation film.	Happy rated 1-10 before and after task	Task BP, HR recovery	Irritated/tense / angry rated 1- 10 before and after task	baseline BP and reactivity	No association between positively valenced film and CV recovery but film did not reliably induce PA state. (Slower BP recovery after negative film, rumination also predicted slow recovery).

ABP=ambulatory blood pressure, HR=heart rate, DBP=diastolic blood pressure, SBP=systolic blood pressure, DRM=Day Reconstruction Method, PA=positive affect, NA=negative affect, PANAS=Positive and Negative Affect Schedule, HF=high frequency, LF=low frequency, HRV=heart rate variability, RSA=respiratory sinus arrhythmia, CAD=coronary heart disease, ERI=Effort Reward Imbalance, GHQ-30=General Health Questionnaire, BDI=Beck Depression Inventory  
Covariates: Ag=age, Sx=sex, Occ=occupational grade or employment status, In=income, Et=ethnicity, BMI=body mass index, WHR=waist hip ratio, PhysAct=frequency of physical activity (self-report), Sm=smoking

*\*\*Indicates where the same study appears in Tables 2.1 and 2.2, reporting different outcomes*



In a much larger study, Brummett et al., (2009) reported that general positive affect was inversely associated with BP reactivity to a task involving recall of a sad event, but not an angry experience. However, the 'general' positive affect measure was calculated based on ratings before, during and after the tasks, so was unlikely to reflect a trait measure of affect. In contrast to the studies above, there was no association between EMA happiness and BP reactivity or recovery to standardised stress tasks in a larger but older sample of men and women from the Whitehall II study (Steptoe et al., 2005).

Two studies attempted to measure the effect of increased positive affect on cardiovascular measures using film clips to induce emotions. Oveis et al. (2009) found a positive association between resting RSA and optimism assessed several months later but the attempt to induce positive mood did not influence RSA. Radstaak et al. (2011) attempted to replicate an earlier series of studies by Fredrickson and colleagues which had reported that viewing amusing films after a negative stressor resulted in faster return to baseline levels than after viewing films to induce sadness or fear (Fredrickson and Levenson, 1998; Tugade et al., 2004). Fredrickson did not simultaneously adjust for both positive and negative emotions so these studies are not included in Table 2.2. Radstaak et al. (2011) did not duplicate Fredrickson's findings; the more negative film was associated with prolonged cardiovascular recovery to a stress task but the positively valenced film failed to reliably induce positive mood or to influence cardiovascular recovery.

#### *Summary of studies assessing well-being and cardiovascular function*

Trait or aggregated EMA measures of positive affect were associated with low cardiovascular activation in most ambulatory studies, but the extent to which this association was statistically independent of negative affect was inconsistent. Differences between studies may be related to the age of the sample, with more consistent ambulatory findings in older populations, and the degree to which specific measures of positive and negative affective measures were independent of one another. Both ambulatory and laboratory studies suggest that highly activated measures of positive affect, such as joy, can also be associated with temporary increases in cardiovascular activity. This is likely to have weakened associations between trait positive affect and lower BP or heart rate when state measures were not taken into consideration.

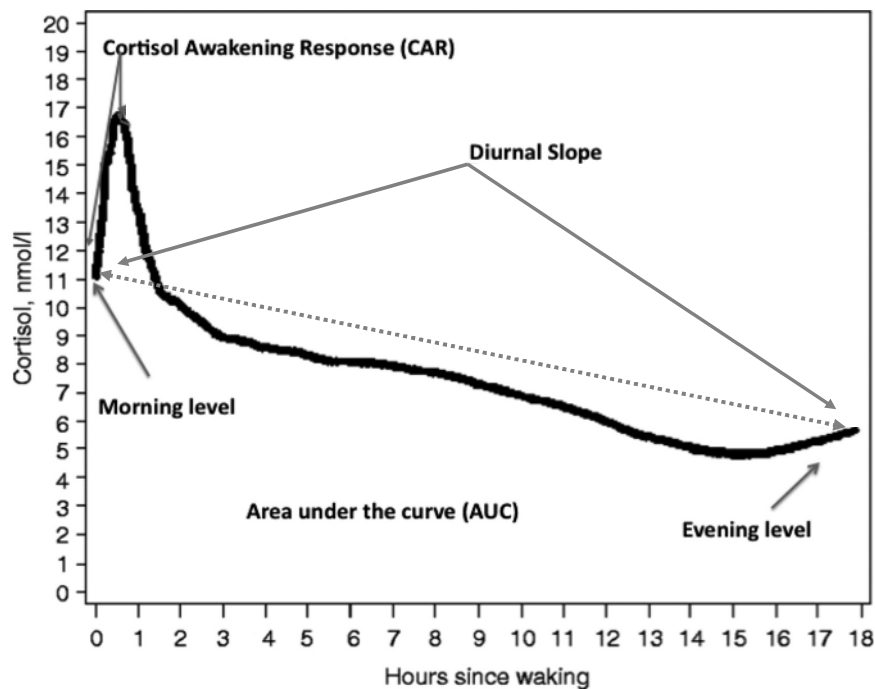
In standardised laboratory studies, three studies in younger populations found that positive affect was associated with accelerated diastolic BP recovery to mental stress, which could be an adaptive response. It remains unclear which measures of subjective well-being or positive emotional experiences are most reliably associated with BP recovery. The absence of this effect in older adults from the Whitehall II study is surprising but associations may change with advancing age. No studies included in the review reported associations between cardiovascular function and eudemonic or evaluative measures of well-being, which might become more important with age. One study in 66 older women found that neither hedonic or eudemonic well-being were associated with resting blood pressure, but this study relied on a single clinic measure of BP and did not adjust for negative affect (Ryff et al., 2006).

### **2.2.3 Salivary cortisol and well-being**

#### *Cortisol as a marker of neuroendocrine function*

Circulating cortisol levels naturally follow a circadian rhythm, peaking rapidly in response to morning waking, declining over the day and rising gradually in the early hours of the morning (Spath-Schwalbe et al., 1992; Wilhelm et al., 2007). The three elements of the diurnal rhythm which have been most frequently studied as indicators of healthy HPA axis function are illustrated in Figure 2.3: the cortisol awakening response or CAR; total cortisol output over the day and the diurnal slope, typically measured as the decline from waking to evening levels (Adam and Kumari, 2009). The CAR is most often calculated as either overall volume of cortisol released over the waking period, measured by integrating the area under the curve imputed from repeated samples (CARauc), or the change (typically increase) of cortisol from the level recorded on waking to 20-45 minutes later (CARi) (Pruessner et al., 2003; Chida and Steptoe, 2009b). Similarly output over the day may be calculated from the area under the curve or the mean of multiple samples taken at timed intervals. Cortisol is routinely determined from blood, salivary or urinary samples in humans but this review focuses on salivary cortisol since this is the least invasive method of measuring circulating cortisol levels and has been used extensively to investigate associations between psychosocial factors and the diurnal cortisol rhythm.

**Figure 2.3** Example of diurnal pattern of cortisol secretion  
extracted from Dowd et al. (2009)



Acute cortisol levels fluctuate markedly depending on a wide array of factors, including acute stress, particularly uncontrollable stress (Dickerson and Kemeny, 2004), nicotine (Steptoe and Ussher, 2006), alcohol consumption (Badrack et al., 2007), food and caffeine (Pincomb et al., 1987; Lovallo et al., 2006). Individuals show considerable within-person variability in cortisol profiles (Stalder et al., 2009). The CAR is typically higher on work days than weekend days (Kunz-Ebrecht et al., 2004a). Waking is a powerful stimulus for morning cortisol so sampling schedules should be based on timed intervals from waking (Wilhelm et al., 2007). A delay between waking and morning samples will lead to a lower CAR (Kunz-Ebrecht et al., 2004a; Dockray et al., 2008). The influence of time of waking on the CAR is debated, with some studies finding no association with waking time (Pruessner et al., 1997; Wust et al., 2000) and some reporting a higher CAR with earlier waking (Kudielka and Kirschbaum, 2003). Two to six days of salivary cortisol sampling have been recommended to reduce the influence of state influences on more stable basal cortisol rhythms (Hellhammer et al., 2007).

Cortisol from the hair shaft has been proposed as a retrospective indicator of mean cortisol exposure over several months (Stalder and Kirschbaum, 2012). Cortisol may passively diffuse into growing hair cells from blood capillaries. Two recent studies have demonstrated

elevated hair cortisol concentrations in patients with cardiovascular disease (Pereg et al., 2011; Manenschiijn et al., 2013). A systematic review found evidence of raised hair cortisol concentrations in people exposed to a range of chronically stressful contexts, but to date no studies have reported associations between hair cortisol and well-being (Staufenbiel et al., 2013).

Cortisol was not included in the review of mechanisms linking well-being and cardiovascular disease by Boehm and Kubzansky (2012) because they argued that cortisol is not reliably linked to cardiovascular outcomes. Since the cut-off for studies included in their review (which included studies by other authors published up to late 2010), several newer studies have strengthened the importance of cortisol as a marker of cardiovascular risk. In the Whitehall II study, raised evening cortisol levels and a flatter diurnal decline over the day predicted increased cardiovascular mortality over six years in a population with a mean age of 61 years (Kumari et al., 2011). Total urinary cortisol over 24 hours also predicted increased cardiovascular mortality risk over six years in a population aged 65 years and above (Vogelzangs et al., 2010). In a controlled laboratory setting, high cortisol responses to mental stress have been shown to predict incident hypertension (Hamer and Steptoe, 2012) and progression of coronary artery calcification (Hamer et al., 2012). The CAR is thought to be controlled independently of cortisol over the remainder of the day and is a response to waking (Clow et al., 2010). High general life stress is typically linked to a high CAR, whereas specific mood disturbances including PTSD and anxiety have been linked to a reduced CAR (Chida and Steptoe, 2009b). It is not clear whether the magnitude of the CAR has long-term prognostic significance for cardiovascular outcomes.

#### *Literature review of positive psychosocial factors and the diurnal cortisol rhythm*

Table 2.3 summarises the findings of studies which have reported the association between positive psychological well-being and cortisol, whilst simultaneously adjusting for negative affect.<sup>10</sup> Fifteen articles were retrieved. Findings are listed in order of cortisol output measure: a) mean daily output, b) awakening response, c) diurnal decline and d) stress reactivity.

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<sup>10</sup> A keyword search in Pubmed and PsycInfo was conducted for empirical studies which measured the association between subjective well-being and cortisol (output over the day, CAR, diurnal decline or evening levels, stress reactivity). Studies were also identified by hand-searching the bibliographies of previous reviews (Pressman and Cohen 2005, Steptoe et al., 2009, Dockray et al., 2010, Chida and

*i) Subjective well-being and cortisol output over the day*

Ten articles reported the association between subjective well-being and cortisol over the day, of which six reported some evidence that positive affect was associated with lower cortisol output and four found no significant associations.

In a large and well-controlled study of over 2,800 adults from the Whitehall II cohort, EMA measures of happiness over a single day were negatively associated with mean cortisol on the same day, independent of psychological distress (Steptoe et al., 2008a). This reinforced the findings of two earlier studies in smaller sub-samples of the Whitehall II cohort in which EMA positive affect predicted low cortisol both in cross-sectional analysis and after three years follow-up (Steptoe and Wardle, 2005; Steptoe et al., 2005). Aggregated measures of positive affect over the day were also related to low mean daily cortisol in 80 Chinese adults (Lai et al., 2005) and in a more rigorously controlled study within 102 working parents in Germany (Nater et al., 2010). Polk et al. (2005) found an association between state but not trait PA in women when cortisol was assessed using a highly intensive protocol (14 samples per day over seven days). Arguably, adhering to such a protocol may have influenced affect. One large study of older adults and two smaller studies in working populations found that negative affect, but not positive affect, independently predicted cortisol levels (van Eck et al., 1996; Jacobs et al., 2007; Steptoe et al., 2007a). However, all three studies omitted the waking sample and two used a cortisol protocol involving random samples, which may not have reliably captured the diurnal rhythm (van Eck et al., 1996; Jacobs et al., 2007). Optimism was not associated with cortisol over the day in the Chinese study or a Whitehall II substudy (Lai et al., 2005; Endrighi et al., 2011).

*ii) Subjective well-being and the cortisol awakening response (CAR)*

Of nine eligible articles, six reported at least partial support for an association between positive emotions and a lower CAR. A case study of one healthy male student over 50 days revealed large intra-individual variability in the awakening response and found an association between prior day, but not same day, happiness and a lower CAR (Stalder et al., 2010). This study had the advantage of excluding between-person influences on the CAR, but results may

not generalise to other individuals or groups. One study in 72 healthy younger men found an association between mean happy ratings over two days and a lower CAR (both area under the curve and increase), but no association with a single retrospective measure of affect based on the PANAS (Steptoe et al., 2007a), reinforcing the importance of experienced affect. Brummett et al. (2009) found that positive affect derived from three separate scales measured before and after a laboratory stress protocol was associated with a lower cortisol increase on awakening (CARi) the preceding day. Two studies reported an association between optimism and the CAR, but one was with the total morning output (CARauc) on work days (Lai et al., 2005) and one was the CARi in middle-aged adults (Endrighi et al., 2011). A trait measure of coping with humour predicted a lower CARauc in older adults (Lai et al., 2010).

In contrast to the findings above, three studies found no association between positive affect and the CAR: positive affect in a small sample of older adults (Evans et al., 2007); EMA happiness ratings on same day CAR in the Whitehall II cohort (Steptoe et al., 2008a) and trait or state affect within in over 300 healthy adults during a 7-day sampling protocol (Polk et al., 2005). Notably none of these three studies specified or adjusted for work or leisure days.

### *iii) Subjective well-being and the diurnal rhythm*

The evidence linking well-being and the steepness of the diurnal decline was very limited with two out of eight studies reporting that positive affect was associated with a low evening cortisol level or a steeper diurnal decline (Simpson et al., 2008; Ong et al., 2011), one study reporting an association with a flatter slope (Polk et al., 2005) and five studies identifying no associations between the diurnal decline and measures of optimism (Lai et al., 2005; Endrighi et al., 2011), EMA positive affect (Steptoe et al., 2007a) or general positive affect (Evans et al., 2007; Steptoe et al., 2007a; Brummett et al., 2009). Studies which reported no effects tended to be based on larger sample sizes than those that found significant associations. The study by Ong and colleagues (2011) was unusual in that positive affect was assessed twice, 12 years apart. The change in positive affect over time associated with the loss of a spouse significantly predicted a flatter diurnal slope compared with control participants, but cross-sectional associations between positive affect and cortisol were not described.

**Table 2.3 Associations between well-being and salivary cortisol over the day**

First author (Date)	Population (nation)	Study design / method	WB measure	Cortisol protocol	NA / stress covariate	Other covariates	Main finding
<b>Cortisol over the day</b>							
Lai (2005)**	80 healthy adults; age 19-50, mean 28y (China)	Association between optimism, PA over the last month and PA on the day with cortisol measured on two work days.	Optimism, Chinese LOT-R PA over the last month (11 emotions rated) & PA on the day of measurement	2 days x 6 samples: waking, +20m, +40m, 1100, 1600, 2100	Pessimism / NA last month, PA & NA on the day of testing	Sx	General PA (last month) associated with low cortisol over the day, after adjusting for NA and mood on the day of testing. No association with optimism, pessimism or NA.
Step toe (2005)	216 healthy working adults aged 47 yr+, Whitehall II cohort (UK)	Association between mean cortisol and mean happiness tested over the same day.	Happy (EMA) rated 1- 5 at each BP inflation (PA), % ratings 4/5 counted	2 days (1 work & 1 leisure) x 8 samples at 2hr intervals from 0800-0830 to 2200- 2230	Psychological distress (GHQ30)	Ag, Occ, BMI, PhysAct, Sm	Higher PA quintile predicted lower mean cortisol over the day on a work day and a leisure day in cross-sectional analysis.
Step toe & Wardle (2005) <i>(follow-up to Step toe 2005,</i> Polk (2005)**	162 adults ( <i>from 216 above</i> ) followed up after 3 years	Longitudinal association between mean happiness and cortisol 3 years later, based on 3 saliva samples over 1 day.	Happy (EMA) rated 1- 5 at each BP inflation (PA), % ratings 4/5 counted	1 day x 3 samples	Psychological distress (GHQ12)	Ag, Occ, BMI, PhysAct, Sm	Borderline sig association between PA (EMA) and mean cortisol (p=0.070) 3 years later.
	334 healthy adults (USA)	Affect assessed on 7 days over 3 weeks to generate trait measures. Associations between trait and state affect with cortisol tested.	PA based on ratings of 9 emotions over the day. Trait=average over 7 days. State=emotion ratings on cortisol measurement day	7 days x 14 samples: 1830, 2230, waking at 545, 0615, 0645, hourly 0800-1600 AUC exc. post waking & post lunch peaks	NA based on 9 emotions, trait and state	Ag, Sx, Et, mean waking time	State PA, but not trait PA, associated with decreased total cortisol concentration in women only. (Trait NA associated with higher cortisol over the day).
Step toe (2008)**	2,873 healthy adults, Whitehall cohort, aged 50+ yrs (UK)	Association between mean daily cortisol and proportion of time spent very/extremely happy over 1 day.	Happy rated on later 4 occasions over the day (counted 'very much/ extremely')	1 day x 6 samples: waking, +30m, +4 times over day and evening ( <i>mean output calculated</i> )	Depression (CES-D)	Ag, Sx, In, Et, Occ, BMI, WHR, Sm, waking time	PA over the day predicted lower mean cortisol over the day, independent of CES-D.

**Table 2.3 Associations between well-being and salivary cortisol over the day (continued)**

First author (Date)	Population (nation)	Study design / method	WB measure	Cortisol protocol	NA / stress covariate	Other covariates	Main finding
<b>Cortisol over the day (cont.)</b>							
Nater (2010)	102 working parents (Germany)	Study designed to assess associations between Big 5, affect and cortisol AUC over the day - tested over 6 days	EMA PA rated 6 times/day: good, alert, relaxed (1-5)	6 days x 6 samples: waking, 0900, 1200, 1500, 1800, 2100	depressive symptoms, neuroticism, conscientious- ness	Sx, BMI, contraceptives, PhysAct, Sm, sleep hours, waking time	Within-person daily PA (not NA) predicted lower daily cortisol. Interaction - association stronger in those with high conscientiousness. (Neuroticism also positively associated with cortisol.)
van Eck (1996)	87 male white collar workers	Association between trait measures of distress and state mood variables with cortisol over five days. Multilevel modelling applied to test state and trait associations.	PA (ESM, 6 emotions) assessed 10 times over the day for 5 consecutive days	5 days x 10 samples at ESM-controlled intervals from 8am to 10pm	NA (ESM), perceived stress, anxiety, depression, life events	Time of day (to adjust for diurnal rhythm), PhysAct, Sm, caffeine, food intake, work or weekend day	No effect of state PA on cortisol. (Distress - state NA and agitation - associated with higher cortisol. Evidence of reduced habituation to NA with higher trait depression.) Only NA independently asssd with cortisol. Minor stressors predicted low PA, high NA and cortisol.
Jacobs (2007)	556 woemn, age 18-61 yrs (Netherlands)	Daily stressors, state mood and cortisol assessed 10 times daily for 5 days. Multilevel modelling tested within-person associations.	PA (cheerful, satisfied, energetic, enthusiastic) rated at the same time as cortisol samples	5 days x 10 samples at random intervals over each day (ESM)	NA, daily stresses	Time of day, recent food or alcohol, smoking, contraceptives	No association between PA (EMA/PANAS) and mean cortisol over the day.
Stephoe (2007)**	72 healthy young men, mean age 33yrs (UK)	Association between EMA PA/PANAS PA and mean cortisol over the day, based on average of 2 working days.	Mean happy rating 4 times over 2 work days (1-5), plus PANAS PA at time of lab session, based on past week	2 work days x 4 samples for for CORTday: 10:30, 12:30, 16:30, 21:30	PANAS NA	Ag, BMI, waking time	No independent association between optimism and AUC over the day.
Endrighi (2011)**	446 healthy adults aged 53+ yrs, Whitehall II cohort (England)	Association between optimism and total area under the curve assessed on 1 day.	Optimism, LOT-R	1 day x 5 samples: waking, +30m, 10am, 4pm, 8pm AUC calculated using trapezoid formula	Depression (CES-D)	Ag, Sx, Occ, BMI, Sm, waking time	No independent association between optimism and AUC over the day.



**Table 2.3 Associations between well-being and the cortisol awakening response**

First author (Date)	Population (nation)	Study design / method	WB measure	Cortisol protocol	NA / stress covariate	Other covariates	Main finding
<b>Cortisol awakening response (CAR)</b>							
Lai (2005)**	80 healthy adults; age 19- 50, mean 28y (China)	Association between optimism, PA over the last month and PA on the day with cortisol measured on two work days.	Optimism, Chinese LOT-R PA over the last month (11 emotions rated) & PA on the day of measurement	2 work days x 3 samples. Morning rise, CARauc, based on waking, waking +20m, waking +40m	Pessimism / NA last month, NA on the day	Sx	Optimism associated with lower CARauc, driven by effect in men. No effect of general PA/PA on the day/NA pessimsim on CARI.
Steptoe (2007)**	72 healthy young men, mean age 33yrs (UK)	Association between EMAN PA/PANAS PA and CARauc/increase measured based on average of 2 working days using regression.	Mean happy rating 4 times over 2 work days (1-5) =EMA PA, plus PANAS PA at time of lab session, based on past week	2 work days x 3 samples for CAR: waking, +30m, +60m	NA (PANAS)	Ag, BMI, waking time	CARauc and CARI inversely associated with PA (EMA). PA (PANAS) not associated with CAR.
Brummett (2009)**	328 healthy young adults, mean age 31y (USA)	Association between general PA assessed in laboratory with CAR on previous day	General PA based on factor analysis of 3 scales, assessed before, during & after lab tasks	1 day x 2 samples for CAR: waking, +30m	General NA	Ag, Sx, In, Et, BMI, Sm	PA significant inverse association with CARI
Lai (2010)	45 healthy older men aged 65+yrs (China)	Association between tendency to cope using humour and CAR assessed over 2 days using regression.	Chinese Humor Scale (tendency to cope with stressful situations with smiling/humour)	2 days x CARauc and CARI calculated from 4 samples: waking, +15m, +30m, +45m	(Socio- economic status)	Ag, self esteem, waking time	Higher scores on coping with humour predicted lower CARauc but no difference in the CARI.
Stalder (2010)	case series: 1 x 27 yr old male (UK)	Test between same day and prior day affect with CAR on 50 measurement days, every third day.	Mood on the day and prior day - happiness rated	50 days x waking, +15m, +30m, +45m, +1hr	Tension	Alertness, obligations, leisure, waking time	22% of the variability in the CAR was accounted for by prior day happiness (inverse association) & sadness, and same day obligations & lack of leisure.

**Table 2.3 Associations between positive well-being and the CAR (continued)**

First author (Date)	Population (nation)	Study design / method	WB measure	Cortisol protocol	NA / stress covariate	Other covariates	Main finding
<b>Cortisol awakening response (CAR) (cont.)</b>							
Endrighi (2011)**	446 healthy adults aged 53+ yrs, Whitehall II cohort (England)	Association between optimism and CAR assessed on one day using regression.	Optimism, LOT-R	1 day x 5 samples: waking, +30m, 10am, 4pm, 8pm CARi = difference between first two samples	Depression (CES-D)	Ag, Sx, Occ, BMI, S, waking time	Optimism associated with a lower CARi (accounted for 1.2% variance) 30% lower CARi in participants with highest vs lowest tertile optimism.
Evans (2007)**	50 older adults mean age 74y (UK)	Association between general PA and NA with diurnal cortisol rhythm assessed over 2 days. Actigraph verification of time of waking.	General PA, based on GHQ-30 positive items	2 consecutive weekdays x 8 samples: CAR based on waking, +15, +30m, +45m	General NA, based on GHQ-30 negative items	Ag, Sx, SES, waking time	No direct main effects of recent PA or NA on CAR. Interaction for low NA and high PA - lower CAR than all other groups.
Polk (2005)**	334 healthy adults (USA)	Affect assessed on 7 days over 3 weeks to generate trait measures. Associations between trait and state affect with cortisol tested using multilevel modelling.	PA based on ratings of 9 emotions over the day. Trait=average over 7 days. State=emotion ratings on cortisol measurement day	7 days x 3 samples. Morning rise, CARi, difference between waking 0545 and higher of 0615/0645	NA based on 9 emotions, trait and state	Ag, Sx, Et, mean waking time	No association between state or trait PA and morning rise in cortisol. (Trait PA associated with low wake-up level in women only).
Stephoe (2008)**	2,873 healthy adults, Whitehall cohort, aged 50+ yrs (England)	Association between CAR and proportion of time spent very/extremely happy over 1 day using regression analyses.	Happy rated on later 4 occasions over the day (counted 'very much/ extremely')	1 day x 2 samples for CAR: waking, +30m CAR based on difference between 2 samples	Depression (CES-D)	Ag, Sx, In, Et, Occ, BMI, WHR, Sm, waking time	No association between CAR and EMA PA.

**Table 2.3 Associations between well-being and the diurnal cortisol slope**

First author (Date)	Population (nation)	Study design / method	WB measure	Cortisol protocol	NA / stress covariate	Other covariates	Main finding
<b>Cortisol diurnal decline, or evening levels</b>							
Simpson (2008)	41 healthy adults aged 55+ yrs (UK)	Associations between afternoon and evening levels of cortisol and concurrent PA/NA and perceived stress tested over 7 days.	Current PA (PANAS), assessed with cortisol	7 days x 2 samples: 1430 and 2230	Perceived stress scale, NA (PANAS)	None	Low afternoon PA predicted higher evening cortisol. No association between NA or perceived stress and cortisol but only bivariate correlations reported.
Ong (2011)	44 older adults, mean age 66y: 22 recently bereaved, 22 matched controls (USA)	Tested hypothesis that changes in PA/NA from 1994 to 2006 would mediate the associations between spousal bereavement (last 3 years) and cortisol rhythm over 4 days.	Recent PA, 6 emotions over past 30 days rated 1-5	4 days x 4 samples waking, +30m, before lunch, bedtime	General NA	Ag, Sx, medication, Sm, extraversion, neuroticism, spousal loss	Spousal loss associated with flatter diurnal curve. Reduction in recent PA over time accounted for 29% of the effect of spousal loss on diurnal slope.
Polk (2005)**	334 healthy adults (USA)	Affect assessed on 7 days over 3 weeks to generate trait measures. Associations between trait and state affect with cortisol tested.	PA (EMA) based on ratings of 9 emotions over the day; Trait=average over 7 days. State=emotion ratings on cortisol measurement day	7 days x 14 samples over 24-hr: 1830, 2230, waking at 545, 0615, 0645, hourly 0800-1600 diurnal decline from 0800 to 1600, excluding post lunch rise	NA based on 9 emotions, trait and state	Ag, Sx, Et, mean waking time	Low trait PA associated with a high flat rhythm in men, low flat rhythm in women. Higher state PA associated with a flatter slope.
Lai (2005)**	80 healthy adults; age 19-50, mean 28y (China)	Association between optimism, PA over the last month and PA on the day with cortisol measured on two work days.	Optimism, Chinese LOT-R PA over the last month (11 emotions rated) & PA on the day of measurement	2 work days x 4 samples for diurnal decline - difference between waking and 1100, 1600 and 2100 samples	Pessimism / NA last month, NA on the day	Gender	No independent association between optimism, PA, NA or pessimism with diurnal decline.
Evans (2007)**	50 older adults, mean age 74y (UK)	Association between general PA and NA with diurnal cortisol rhythm assessed over 2 days. Actigraph verification of time of waking.	General PA, based on GHQ-30 positive items	2 consecutive weekdays. Diurnal decline based on waking, +3, +6, +9, +12hr	General NA, based on GHQ-30 negative items	Ag, Sx, SES, waking time	No association between general PA or NA with any pm cortisol measure or slope

**Table 2.3 Associations between well-being and the diurnal cortisol slope or reactivity**

First author (Date)	Population (nation)	Study design / method	WB measure	Cortisol protocol	NA / stress covariate	Other covariates	Main finding
<b>Cortisol diurnal decline, or evening levels</b>							
Stephoe (2007)**	72 healthy young men, mean age 33yrs (UK)	Association between EMA PA/PANAS PA and diurnal decline measured based on average of 2 working days.	Mean happy rating 4 times over 2 work days (1-5) =PA (EMA), plus PA (PANAS) at time of lab session, based	2 working days (samples for slope of diurnal decline not specified)	NA (PANAS)	Ag, BMI, waking time	No association between PA (EMA/PANAS) and diurnal decline.
Brummett (2009)**	328 healthy young adults, mean age 31y (USA)	Association between general PA assessed in laboratory with cortisol decline on the previous day	General PA based on factor analysis of 3 scales, assessed before, during & after lab tasks	1 day x 2 samples for decline - difference between bedtime and waking sample	General NA	Ag, Sx, In, Et, BMI, Sm	No association between PA and magnitude of decline over the day
Endrighi (2011)**	446 healthy adults aged 53+ yrs, Whitehall II cohort (England)	Association between optimism and diurnal decline assessed on one day	Optimism, LOT-R	1 day x 5 samples: waking, +30m, 10am, 4pm, 8pm Diurnal slope based on regression slope	Depression (CES-D)	Ag, Sx, Occ, BMI, Sm, waking time	No independent association between optimism and decline over the day.
<b>Laboratory stress reactivity and recovery</b>							
Endrighi (2011)**	446 healthy adults aged 53+ yrs, Whitehall II cohort (England)	Association between optimism and cortisol responses to two mental stress tasks	Optimism, LOT-R	Lab: cortisol assessed at baseline, post-task, 20, 45, 75min later AUC, reactivity and recovery calculated	Depression (CES-D)	Ag, Sx, Occ, BMI, Sm, waking time	Optimism was not significantly associated with cortisol AUC, reactivity or recovery (was associated with lower perceived stress during task).

ABP=ambulatory blood pressure, HR=heart rate, DBP=diastolic blood pressure, SBP=systolic blood pressure, DRM=Day Reconstruction Method, PA=positive affect, NA=negative affect, PANAS=Positive and Negative Affect Schedule, HF=high frequency, LF=low frequency, HRV=heart rate variability, RSA=respiratory sinus arrhythmia, CAD=coronary heart disease, ERI=Effort Reward Imbalance, GHQ-30=General Health Questionnaire, BDI=Beck Depression Inventory  
Covariates: Ag=age, Sx=sex, Occ=occupational grade or employment status, In=income, Et=ethnicity, BMI=body mass index, WHR=waist hip ratio, PhysAct=frequency of physical activity (self-report), Sm=smoking

**\*\*Indicates where the same study appears in the table more than once, reporting different outcomes**

#### *iv) Subjective well-being and cortisol stress reactivity*

Endrighi et al. (2011) found no relationship between optimism and cortisol reactivity or recovery to two standardised mental stress tasks in 446 men and women from the Whitehall II cohort. Interestingly, optimism was associated with lower subjective stress during the tasks, despite the finding in previous studies from our research group that positive affect measured via EMA ratings was not associated with subjective stress during laboratory tasks in either a Whitehall II substudy or a smaller study within 72 young men (Steptoe et al., 2005; Steptoe et al., 2007a).

#### *Summary of studies assessing well-being and cortisol*

The evidence linking cortisol and subjective well-being is relatively inconsistent, but the balance of evidence suggests a weak association between experienced positive affect and low mean cortisol output on the same day and a lower cortisol awakening response. Evidence linking high negative affect with heightened cortisol over the day appeared to be more consistent than the association with positive affect. These results are in line with a meta-analytic review of factors associated with the CAR which found that positive psychosocial factors did not have a reliable association with cortisol (Chida and Steptoe, 2009b).

It may be that well-being is not directly associated with the diurnal rhythm, but it is also possible that methodological limitations have contributed to the inconsistency of findings. Self-monitoring studies have an advantage of ecological validity but it is not possible to control exposure to daily stressors. With the exception of one study, all studies relied on self-reported waking times and sampling times for salivary cortisol, which may have introduced inaccuracies (Evans et al., 2007). Few studies adjusted for dietary influences or smoking, which can influence cortisol levels (Adam and Kumari, 2009). Notably three of the four studies which found no association between cortisol and affect over the day did not include the waking sample (van Eck et al., 1996; Jacobs et al., 2007; Steptoe et al., 2007a), which has a critical influence on the diurnal rhythm (Adam and Kumari, 2009). To reduce the variability in exposures to stress and behavioural covariates, further studies using a standardised laboratory protocol are warranted to investigate associations between measures of well-being and acute cortisol stress reactivity.

Another limitation is the lack of longitudinal studies: only one study assessed cortisol on more than one occasion, revealing a borderline significant association between EMA positive affect and mean daily cortisol three years later (Steptoe and Wardle, 2005). To date the majority of studies have used state positive affect as an indicator of psychological well-being. Several studies found an association between cortisol and either state or trait positive affect, but the significant associations varied between studies. Optimism was unrelated to cortisol over the day or cortisol stress reactivity but was associated with a low CAR in two studies. Further research is needed to clarify associations between specific well-being indicators and cortisol indicators. None of the reviewed studies investigated whether evaluative or eudemonic aspects of well-being were associated with cortisol.

#### **2.2.4 Subjective well-being and other biomarkers**

This section highlights key evidence relating to immune, inflammatory and metabolic systems. The relationships between positive psychological well-being and other biomarkers have been reviewed in more detail by Boehm and Kubzansky (2012).

##### *Immune system*

Inflammatory and immune mechanisms play a key role in the development of atherosclerosis (Galkina and Ley, 2009). A review by Marsland et al. (2007) highlighted favourable links between positive affect and the number and function of immune cells. Dispositional positive affect predicted a greater antibody response to hepatitis B vaccination administered to 84 students (Marsland et al., 2006). Cohen et al. (2006a) inoculated over 330 healthy volunteers with rhinovirus and monitored participants under controlled conditions for three weeks. Daily measures of affect aggregated into a trait measure of positive emotional style predicted lower likelihood of developing symptoms of infection, in a dose-response relationship. The results reported in the studies by Cohen (2006) and Marsland (2006) were independent of a large number of covariates including negative affect. Brydon et al. (2010) inoculated 29 healthy men with typhoid vaccine prior to a laboratory mental stress protocol to show that trait optimism predicted an enhanced antibody response to the immune challenge in the context of acute stress. Importantly, optimists reported lower negative affect and higher mental vigour during the tasks.

## *Inflammation*

The pro-inflammatory cytokine, IL-6, is involved in leukocyte and endothelial cell activation and high circulating levels predict CHD and cardiovascular mortality (Noto et al., 2007; Fan et al., 2011). Elevated IL-6 also predicts incident type 2 diabetes (Pradhan et al., 2001). There is some evidence that both hedonic and eudemonic measures of well-being are inversely associated with inflammation, with more consistent evidence in women. In over 3,000 middle-aged adults from the Whitehall II cohort, EMA positive affect was associated with plasma IL-6 and C-reactive protein after adjusting for depressive symptoms, but only in women (Steptoe et al., 2008b). Steptoe et al. (2012) also reported that hedonic and eudemonic measures of well-being were associated with low C-reactive protein and fibrinogen in women, but not men, from the English Longitudinal Study of Ageing (ELSA), independent of a number of baseline health measures including depressive symptoms, arthritis, coronary heart disease and limiting long-standing illness. Optimism was correlated with low levels of IL-6, C-reactive protein and fibrinogen in both men and women in cross-sectional analysis of the Multi-Ethnic Study of Atherosclerosis, but after adjustment for pessimism, depressive symptoms and chronic illness, only an inverse association between pessimism and fibrinogen remained significant (Roy et al., 2010). Control for depressive symptoms is particularly important since inflammatory cytokines are known to induce negative mood (Wright et al., 2005).

Inflammatory markers can also be assessed in response to acute psychosocial stress, although IL-6 may take several hours to respond (Steptoe et al., 2007b). In the typhoid vaccine study by Brydon and colleagues (2010), optimism was associated with reduced IL-6 responses to mental stress tasks in both typhoid vaccine and no-vaccine groups. An in vitro study within 146 middle-aged adults found that trait positive affect based on the PANAS predicted decreased production of both IL-6 and IL-10 in response to stimulation with endotoxin, independent of negative affective style (Prather et al., 2007). Aschbacher et al. (2012) reported that in 35 women subjected to the Trier Social Stress Test, those that maintained a positive outlook had reduced IL-1 $\beta$  reactivity to the task. IL-1 $\beta$  is a stress-responsive cytokine which regulates IL-6. Our group also found that stress-induced increases in fibrinogen, a haemostatic marker involved in atherosclerotic processes, were lower and less prolonged in individuals with higher EMA affect over the day, independent of psychological distress (Steptoe et al., 2005).

### *Atherosclerosis*

In spite of the evidence linking measures of subjective well-being to low levels of inflammatory markers, studies examining associations with atherosclerosis have reported inconsistent findings. Matthews et al. (2006) reported that the eudemonic measures of mastery and life engagement were inversely associated with aortic calcification but not with coronary artery calcification (CAC) in 155 post-menopausal women. In a follow-up of the same cohort, an index derived from negative psychosocial factors (depression, stress, cynicism) predicted progression of CAC, whereas positive psychological resources (including optimism, purpose in life, self-esteem) had no association with the progression of subclinical atherosclerosis (Low et al., 2011). Experienced affect over the day may have greater predictive value for progression of coronary artery disease. Kroenke et al. (2012) found that higher average positive mood over the day, assessed by momentary assessment, predicted CAC independent of depressive symptoms. A pattern of improving mood over the day had a stronger association with prevalent CAC. However, over five years, only a pattern of worsening negative mood over the day was significantly associated with progression of CAC.

### *Metabolic markers*

Metabolic markers of increased cardiovascular risk include high glycosylated haemoglobin (HbA1c, a measure of blood glucose control over time), total cholesterol, low-density lipoprotein (LDL) cholesterol, body mass index (BMI) and triglycerides (Abraham et al., 2007). High-density lipoprotein (HDL) cholesterol is associated with reduced CVD risk. A recent cross-sectional study of 990 healthy middle-aged adults found that optimism was associated with higher HDL-cholesterol and low triglycerides with a magnitude of association similar to physical activity, independent of behavioural factors, health status or negative affect. There was no association between optimism and total or LDL cholesterol (Boehm et al., 2013b). Within the ELSA cohort, eudemonic and hedonic measures of well-being were associated with low triglycerides in men and women. Well-being measures were also associated with higher HDL cholesterol in women (Steptoe et al., 2012).

Tsenkova et al. (2008) reported that positive affect predicted low HbA1c in older women after two years follow-up, after controlling for baseline levels and negative affect. In the same study, eudemonic well-being did not predict HbA1c. Cross-sectional studies have



also reported null associations between hedonic and eudemonic well-being and HbA1c (Feldman and Steptoe, 2003; Paschalides et al., 2004).

A number of cross-sectional studies have found an inverse association between BMI and hedonic or eudemonic well-being (Carr and Friedman, 2005; Saloumi and Plourde, 2010), but there is evidence that these associations can be moderated by social skills and social support (Dierk et al., 2006). Longitudinal studies have been inconclusive with some studies finding that well-being is associated with reduced risks of weight gain and others reporting null results. For example, the eudemonic construct locus of control in childhood predicted reduced risks of being overweight or obese 20 years later in the 1970 British Cohort Study (Gale et al., 2008). Low life satisfaction in a Finnish twin study was associated with weight gain six years later in older women, but not in younger women or men (Korkeila et al., 1998).

#### *Telomere length*

Telomeres are repetitive DNA sequences that cap chromosomal ends and play a critical role in chromosomal stability (Blackburn, 2001). Telomeres shorten with every cell division. Telomere length, which is regulated by the cellular environment, has emerged as an index of cellular aging. Perceived and chronic environmental stressors have been linked to higher oxidative stress, lower telomerase activity and shorter telomere length (Epel et al., 2004). O'Donovan et al. (2012) showed that optimism was correlated with longer telomere length in postmenopausal women, but the effect was no longer significant after controlling for caregiver stress and pessimism. More recently, Rius-Ottenheim et al. (2012) found no independent association between well-being and telomere length in a study of elderly men.

#### **2.2.5 Summary of psychobiological studies and implications for this thesis**

The evidence discussed in this chapter tentatively supports an association between positive emotional well-being and lower daily cardiovascular arousal, accelerated cardiovascular recovery to acute stress, reduced daily cortisol release, a lower cortisol awakening response, increased immune function, reduced inflammatory markers and a healthier metabolic profile. Measures of negative affect tended to have opposite associations with biological markers and the extent to which positive and negative affect had independent effects varied by study.

It remains unclear which well-being indicators have the strongest and most consistent associations with biological markers. Trait measures of positive affect had a more consistent association with low cardiovascular activation than state measures, but state positive affect appeared to be a more consistent predictor of cortisol over the day. Puzzlingly, trait optimism, which had a consistent association with reduced risks of CVD in prospective studies reviewed in Chapter 1, was not reliably associated with cardiovascular function, cortisol over the day or atherosclerosis. Steptoe et al. (2007a) proposed that repeated EMA measures of positive affect based on current experience would be more closely aligned to dynamic biological mechanisms than single retrospective accounts. Daly (2012) also found that momentary positive affect was a better predictor of mortality than recalled feelings of well-being. Associations between different measures of psychological well-being and cortisol and blood pressure are considered in Chapters 3 and 8.

Measures of positive well-being are inversely associated with negative affect and perceived stress, but few studies have investigated whether this is due to differences in stress exposure or differences in conscious cognitive perceptions. Laboratory stress testing enables individual differences in the perceptions of standardised stressors to be compared in a controlled environment. Two studies from our group found no association between EMA ratings of happiness over one or two days and perceptions of control or subjective stress during mental stress tasks (Steptoe et al., 2005; Steptoe et al., 2007a). In contrast, trait positive affect was associated with more rapid recovery of subjective tension after an exam-style stressor (Papousek et al., 2010) and optimism predicted lower perceived stress and greater task control during two mental stress tasks (Brydon et al., 2009). The association between positive affect and cognitive perceptions of an acute stress task are investigated in Chapter 3.

The role of exposure to chronic stress in the relationship between measures of positive affect and biological markers has received very little attention to date. Only one of the studies reviewed in Tables 2.1, 2.2 and 2.3 adjusted for work stress, despite evidence from meta-analyses that work stress is associated with elevated ambulatory blood pressure and a heightened cortisol awakening response (Chida and Steptoe, 2009b; Landsbergis et al., 2013).

The relationship between psychological well-being and chronic environmental stress is discussed in more detail in Chapter 4 and investigated in Chapters 5, 6 and 8.

The vast majority of the evidence reviewed in this chapter was based on cross-sectional analyses. A small number of studies documented associations between naturally occurring variation in well-being and biological markers over time but none of these studies deliberately attempted to influence well-being. Chapter 7 considers whether interventions which aim to increase well-being are associated with changes in biological systems.

## **Chapter 3 Positive emotional style and subjective, cardiovascular and cortisol responses to acute laboratory stress**

This chapter describes an experiment which set out to address some of the gaps identified in the literature review in Chapter 2. I investigated associations between a dispositional measure of positive emotional experience, termed 'positive emotional style', and task appraisals, cardiovascular and cortisol responses to standardised mental stress tasks in the laboratory. The results have been published in *Psychoneuroendocrinology* (Bostock et al., 2011).

### **3.1 Introduction**

This study aimed to compare associations between two alternative measures of positive affect with subjective, cardiovascular and cortisol responses to acute mental stress. In Chapter 2, I suggested that subjective well-being might influence stress responses at the level of cognitive appraisals of stressors or coping resources. Tugade and Fredrickson (2004) demonstrated that students scoring highly on resiliency, a measure of ability to adapt flexibly to changing circumstances, were more likely to appraise a speech task as a challenge than a threat. Resilient individuals maintained higher levels of positive emotions during the task, which mediated faster post-stress cardiovascular recovery. Papousek et al. (2010) found that students higher in trait positive affect reported less subjective tension during a mock exam stressor. Endrighi et al. (2011) similarly reported that trait optimism predicted lower subjective stress and greater control during two mental stress tasks. However, two studies found no association between experienced EMA measures of happiness and task appraisals, despite significant associations with acute biological stress responses (Steptoe et al., 2005; Steptoe et al., 2007a). I hypothesised that a measure designed to assess dispositional positive emotional experience would be associated with positive appraisals of two mental stress tasks, regardless of task performance.

The review in section 2.2.2 identified three studies in young adults in which positive affect predicted accelerated blood pressure (BP) recovery from mental stress (Steptoe et al., 2007a; Dowd et al., 2010; Papousek et al., 2010), one study which found an association with reduced reactivity (Brummett et al., 2009) and one study in middle-aged adults with no BP

response effects (Steptoe et al., 2005). Both heightened BP reactivity and delayed recovery have been related to increased CHD risk (Chida and Steptoe, 2010). Building on a previous study from our group which identified an association between EMA affect and BP recovery in young men (Steptoe et al., 2007a), the current study tested the association between dispositional positive affect and acute stress responses in young women. Laboratory tasks that are perceived to be uncontrollable or characterised by social-evaluative threat have been shown to increase cortisol release (Dickerson and Kemeny, 2004). The relationship between well-being and acute salivary cortisol responses has so far received little attention (Endrighi et al., 2011). I hypothesised that dispositional positive emotions would be associated with both rapid BP and cortisol recovery from two standardised mentally challenging tasks designed to promote an acute stress response: a speech task and a mirror tracing task.

Steptoe et al. (2007a) demonstrated that a measure of recalled positive affect over the past week had weaker associations with biological stress responses than happiness derived from ecological momentary assessment (EMA). Measures aggregated over several occasions during the day or across days may provide more reliable estimates of typical affective traits, since they may be less prone to recall bias, brief peak moods and the dominance of current affect (Kahneman et al., 2006). EMA involves a relatively heavy participant burden, which may limit its suitability for certain populations. The third aim of this study was to trial a once-a-day mood rating scale to provide an aggregated measure of experienced hedonic positive affect. We collected affect ratings every evening over seven days through the Internet, and computed aggregated mean daily positive affect ratings termed 'positive emotional style', or PES. I hypothesised that PES over seven days would correlate more closely with biological stress responses than a more evaluative measure based on retrospective positive affect over the past few days assessed by the Profile of Mood States (POMS) mental vigour scale (McNair et al., 1971).

To establish whether associations between positive affect and biology were independent of negative affect, I adjusted for two alternative measures of negative affect: the negative items from the POMS and depressive symptoms measured with the Centre for Epidemiological Studies Depression Scale (CES-D)(Radloff, 1977).

### 3.1.1 Hypotheses

- Hypothesis 1: Higher positive emotional style (PES) will be associated with lower perceived stress during the tasks.
- Hypothesis 2: PES will be associated with more rapid blood pressure recovery following the tasks.
- Hypothesis 3: PES will be associated with faster cortisol recovery following the tasks. The associations in hypotheses 1-3 will each be independent of depressive symptoms.
- Hypothesis 4: PES assessed over seven days will correlate more closely with biological stress responses than a single measure of recalled affect based on the last few days.

### 3.1.2 Methods

#### *Participants*

Forty women aged 21-45 years were recruited from the staff and student population of University College London (UCL). Recruitment posters with contact details for the research team were displayed around the campus. Interested applicants were sent a study information form and screened for eligibility by phone. The study was confined to women to avoid gender influences on cortisol stress responses (Maruyama et al., 2012). Participants were non-smokers, consumed fewer than 14 units of alcohol per week and reported being in good health at the time of the study. Women taking prescription medications, excluding contraception, were excluded from the study. Psychophysiological stress responses tend to be greater in individuals experiencing a higher background level of general stress (Chida and Hamer, 2008), so women with very low scores (<2) on the 12-item General Health Questionnaire (Goldberg et al., 1997) were also excluded. Participants gave written consent to participate in the study and ethical approval was obtained from UCL ethics committee. Participants were given an honorarium of £30 on completion.

#### *Procedure*

Eligible participants attended a face to face meeting at which they were instructed to record their mood using an online questionnaire at the end of the day for seven days preceding the laboratory stress session. On the day of testing, participants were instructed not to have drunk caffeinated beverages or eaten large meals at least two hours before the study and not

to have consumed alcohol or exercised on the previous evening (Lovallo et al., 2006). Participants who reported colds or other infections on the day of testing were re-scheduled. Testing was completed individually in a light and temperature-controlled laboratory between 1200 h and 1700 h. Physical measurements including height, weight, percentage body fat, waist and hip circumference were made using standardised methods, and body mass index (BMI) was calculated. Participants rinsed their mouths to avoid contamination of saliva samples. Blood pressure and heart rate (HR) were monitored continuously from the finger using a Finometer (TNO Biomedical Instrumentation, Amsterdam, Netherlands) which uses the vascular unloading technique.

Participants completed a questionnaire at rest. After a further 45-minute rest period spent sitting quietly, 5-minute 'baseline' blood pressure and HR readings were taken followed by a saliva sample. Cardiovascular readings continued during two 5-minute standardised behavioural challenges in random order: a mirror tracing task and a socially evaluating speech task. Cardiovascular responses to these standardised tasks had previously been linked to positive affect (Steptoe et al., 2007a). In the speech task participants were given a hypothetical scenario in which they had to verbally defend themselves against the threat of unemployment. They were given two minutes to prepare and then asked to speak into a video camera for three minutes. Participants were told that the tape would later be replayed by the research team and evaluated. The mirror tracing task involved making as few mistakes as possible whilst tracing a star which could only be seen in a mirror image. Participants were told that the numbers of mistakes and completed tracings would be recorded. Each task was immediately followed by task ratings of perceived stress, difficulty, control, performance and involvement. Saliva was collected after completion of the second task. After 20-minutes spent reading quietly, 5-minute cardiovascular 'recovery' readings and a final saliva sample were taken. Subjective ratings of stress (tension) were also recorded at baseline, post-tasks and recovery. A summary of the laboratory study protocol and all key measures are included in the Appendix for Chapter 3.

### *Measures*

Positive emotional style (PES) was assessed using an online daily mood rating scale completed every evening for seven days. The scale was an abridged version of a questionnaire used previously to link PES to reduced vulnerability to the cold virus (Cohen et al., 2003),

higher antibody responses to a vaccine (Marsland et al., 2006), and reduced daily cortisol output (Polk et al., 2005). Participants were asked to rate the degree to which they felt a number of emotions during that day on a 5-point Likert scale, ranging from 0 'you haven't felt this at all today' to 4 'you felt this way a lot today'. PES was defined as the mean daily score for positive emotions comprising subscales for well-being (happy, cheerful); vigour (lively, full of pep) and calm (calm, at ease). Multiple entries on a single day or morning entries were excluded. All participants completed a minimum of 5 valid daily questionnaires (mean 6.9). Internal consistency based on Cronbach's  $\alpha$  for PES was 0.89.

Task impact ratings of perceived difficulty, involvement, performance, and control were obtained after each task on 7-point Likert scale, from 1 'not at all' to 7 'very'. Subjective ratings of current stress (tension) were also scored on 7-point scales.

Retrospective measures of affect based on a time frame of 'the last few days' were measured before the laboratory tasks using a short form of the POMS (McNair et al., 1971), described previously (Steptoe et al., 1989). Items were rated from 0–4, with higher scores indicating more intense mood. Six positive items contributed to the mental vigour scale ( $\alpha=0.85$ ), while 30 negative items made up the measure of negative affect ( $\alpha=0.94$ ). Scores for both POMS vigour and POMS negative affect could range from 0–24. Depressive symptoms in the past week were assessed with the Centre for Epidemiological Studies Depression Scale (CES-D) (Cronbach  $\alpha=0.83$ ) (Radloff, 1977).

Saliva samples were collected using a passive drool technique. Saliva was decanted into standard centrifugation tubes and frozen immediately ( $-80^{\circ}\text{C}$ ). On completion of the study sessions, salivary cortisol was measured via enzyme-linked immunosorbent assay (ELISA) (SLV-2930, DRG International, Inc., USA) at Technical University Dresden, Germany. The intra- and inter-assay coefficients of variation were less than 8%.

### *Statistical analysis*

Forty volunteers completed the daily mood questionnaires and subjective ratings during the laboratory stress session. Complete cortisol data were available for 35 participants and complete blood pressure data were available for 31 participants owing to equipment faults. BP and HR were averaged into baseline, speech task, mirror task and recovery trials. BP



recovery was scored as the difference between levels during the 20 to 25 minute post-task recovery trial and baseline; more positive scores therefore indicate delayed (incomplete) recovery. Reactivity was calculated by subtracting the baseline values from the mean values measured during the mirror and speech tasks. Cortisol release at baseline, post-tasks and recovery were transformed using natural logarithms to improve the fit to the normal distribution. Raw values are presented in the tables and figures.

Mean PES approximated a normal distribution. Bivariate Pearson correlations were used to examine the associations between PES and normally distributed baseline characteristics. To illustrate the differences between subjects with higher and lower PES, subjects were divided at the median value to compare high and low PES groups. Mean baseline characteristics were compared using t-tests.

Overall patterns of blood pressure, heart rate, cortisol release (logarithmic transformation) and subjective stress response over the time course of the experiment were analysed with a series of repeated measures analyses of variance (ANOVAs) with PES group (high, low) as the between person factor and trial (baseline, tasks, recovery) as the within-subject factor. The Greenhouse Geisser correction for degrees of freedom was applied where appropriate. Focused linear regression analyses were then used to examine the relationship between PES and task ratings, cortisol release, cardiovascular stress reactivity and recovery at the different trials. Reactivity and recovery regression models were adjusted for baseline levels of the relevant measure, age and BMI. Negative affective items from the POMS were subsequently added as a covariate to each model. These analyses were repeated by replacing POMS negative affect with CES-D to ensure that depressive symptoms were controlled for. Repeated measures analyses of variance and regression analyses were repeated using the POMS mental vigour scale as the between-person factor. Regression results are presented as un-standardised ( $\beta$ ) regression coefficients with 95% confidence intervals. Mean values are presented  $\pm$  standard deviations. Analyses were conducted using SPSS version 16.

## 3.2 Results

### *Participant characteristics*

Seven day aggregate PES ratings ranged from 0.86 to 3.36. All participants were at risk of medium to high levels of psychological distress, with GHQ-12 scores between 3 and 12 (mean score  $7.5 \pm 2.8$ ). Table 3.1 illustrates the differences between subjects higher and lower in PES, divided at the median. PES was not correlated with age, BMI, waist circumference, resting blood pressure, heart rate, cortisol or self-rated tension. The three PES subscales (well-being, vigour and calm) were significantly correlated with one another ( $r=0.55-0.70$ ). Higher PES was strongly correlated with higher POMS vigour scores ( $r=0.48$ ,  $p=0.002$ ) inversely correlated with POMS negative affect ( $r=-0.49$ ,  $p=0.002$ ) and CES-D scores ( $r=-0.54$ ,  $p<0.001$ ).

**Table 3.1 Baseline characteristics of subjects with lower and higher PES**  
Mean score (standard deviation) and correlations with PES continuous scores

	Positive Emotional Style (PES)		Correlation with mean PES, r
	Low (n=20)	High (n=20)	(n=40)
Age	28.6 $\pm$ 6.6	29.0 $\pm$ 5.6	0.073
BMI	23.4 $\pm$ 4.8	22.7 $\pm$ 4.0	0.060
Waist circumference, cm	74.5 $\pm$ 12.6	74.0 $\pm$ 8.1	0.046
Diastolic BP, mmHg <sup>\$</sup>	74.5 $\pm$ 9.9	69.2 $\pm$ 7.5	-0.127
Systolic BP, mmHg <sup>\$</sup>	114.5 $\pm$ 13.6	116.3 $\pm$ 14.6	0.248
Heart rate, bpm <sup>\$</sup>	69.4 $\pm$ 9.9	65.9 $\pm$ 7.9	-0.120
Cortisol (log), nmol/l <sup>^</sup>	1.53 $\pm$ 0.6	1.41 $\pm$ 0.4	-0.192
Self-rated tension	1.60 $\pm$ 1.3	1.85 $\pm$ 1.1	0.008
POMS-vigour	8.6 $\pm$ 4.3	<b>11.7 <math>\pm</math> 3.8<sup>a</sup></b>	<b>0.476*</b>
POMS-negative affect	8.4 $\pm$ 3.8	<b>5.0 <math>\pm</math> 2.7<sup>a</sup></b>	<b>-0.485*</b>
CES-D	19.4 $\pm$ 7.4	<b>12.4 <math>\pm</math> 6.6<sup>a</sup></b>	<b>-0.544*</b>
PES score	1.66 $\pm$ 0.37	2.52 $\pm$ 0.35	1

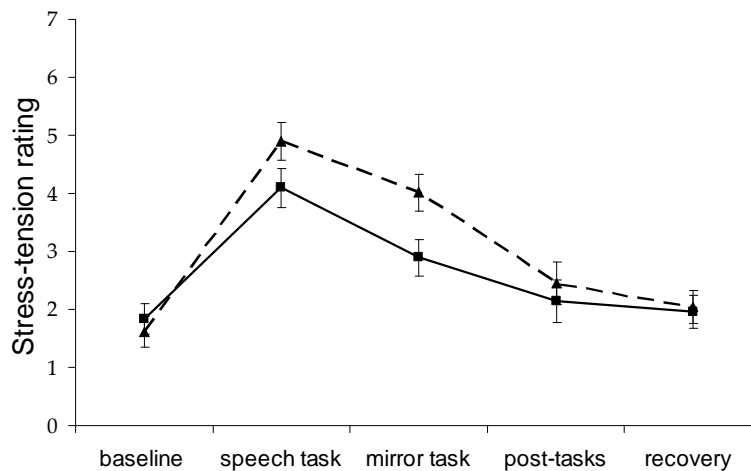
<sup>a</sup>Significant difference between high and low PES groups ( $p\leq 0.05$ );

\*Pearson correlation coefficient significant ( $p\leq 0.01$ ); <sup>\$</sup>n=31, <sup>^</sup>n=35

### 3.2.1 Hypothesis 1: Higher PES will be associated with lower subjective stress

A repeated measures ANOVA on subjective tension ratings revealed a significant group by trial quadratic effect ( $F(1,38)=4.92, p=0.033$ ), illustrated in Figure 3.1. PES was not associated with baseline or recovery levels of subjective tension, but during the tasks, participants with higher PES experienced lower subjective tension ( $B= -0.935$ , C.I.  $-1.683$  to  $-0.186$ ,  $p=0.016$ ) after adjustment for baseline stress levels, age, BMI and POMS negative affect. Positive emotional style accounted for 11.8% of the variance in tension during tasks. Similar results were found when CES-D replaced POMS negative affect in the model ( $B= -1.040$ , C.I.  $-1.809$  to  $-0.270$ ,  $p=0.010$ ). Individuals with greater PES were therefore less subjectively stressed by tasks, even after negative affect had been taken into account. Importantly PES was not significantly associated with task involvement or objective measures of mirror task performance (number of tracings or errors).

**Figure 3.1 Subjective stress/tension levels for high and low PES groups**  
High PES (solid line) and low PES groups (dotted line) during baseline, speech and mirror tasks and recovery. Error bars represent standard error of mean; adjusted for age and BMI (n=40).



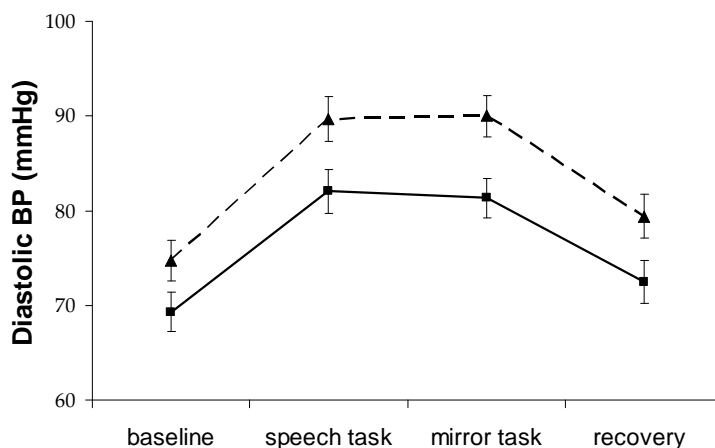
Regression analyses also showed associations between higher PES and lower task difficulty ( $B= -0.677$ , C.I.  $-0.010$  to  $-1.343$ ,  $p=0.047$ ) and greater task control ( $B= 1.054$ , C.I.  $0.230$  to  $1.878$ ,  $p=0.014$ ), adjusted for age, BMI and POMS negative affect. POMS vigour was not significantly associated with subjective tension ( $B= -0.092$ , C.I.  $-0.186$  to  $-0.002$ ,  $p=0.055$ ) or other subjective ratings during the task, or at any other phase of the experiment.

### 3.2.2 Hypothesis 2: Higher PES will be associated with rapid BP recovery

The tasks elicited increases in BP of approximately 20%. Repeated measures analysis of variance confirmed within-subjects main effects of trial for systolic BP, diastolic BP and HR ( $F(3, 87) = 80.1, 114.3$  and  $79.4$ ,  $p < 0.001$ ). Recovery at 20-25 minutes was incomplete, with a mean difference between baseline and recovery of 6.9 mmHg for systolic BP (95% C.I. 4.2 to 9.6) and 4.0 mmHg for diastolic BP (95% C.I. 2.5 to 5.4).

There was a significant group by trial cubic effect in the analysis of diastolic BP illustrated in Figure 3.2 ( $F(1,29) = 4.95$ ,  $p = 0.034$ ). Greater PES was associated with more effective diastolic BP recovery, after adjusting for baseline diastolic BP, age, BMI and negative affect ( $B = -3.051$ , C.I. -5.270 to -0.382,  $p = 0.027$ ; Table 3). Inclusion of PES in the model independently accounted for 16.3% of the variance in diastolic BP recovery. This association was maintained after adjusting for depressive symptoms instead of POMS negative affect ( $B = -2.689$ , C.I. -5.365 to -0.013,  $p = 0.049$ ). There was a similar group by trial cubic interaction for PES and systolic BP ( $F(1,29) = 4.28$ ,  $p = 0.048$ ), but in this case the systolic BP recovery difference was not significant after adjusting for covariates ( $p = 0.081$ ). PES was not related to systolic or diastolic BP reactivity.

**Figure 3.2 Diastolic BP stress responses for high and low PES groups**  
PES (solid line) and low PES groups (dotted line) during baseline, speech and mirror tasks and recovery. Error bars represent standard error of mean; adjusted for age and BMI ( $n = 31$ ).



POMS vigour was also associated with more effective diastolic BP recovery after controlling for baseline diastolic BP, age, gender and negative affect (B= -0.386, C.I. -0.739 to -0.032, p=0.034). The relationship with recovery did not persist after adjusting for depressive symptoms (B = -0.342, C.I. -0.707 to -0.023, p=0.065). POMS vigour was not related to systolic BP over time, reactivity or recovery. Neither PES nor POMS vigour were related to heart rate reactivity or recovery. Subjective task ratings were not significantly correlated with BP reactivity or recovery.

**Table 3.2 Summary of key linear regression results**

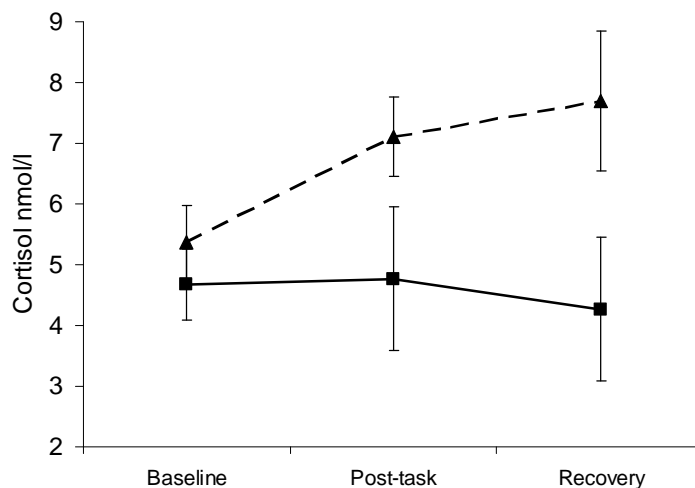
	<b>β Regression Coefficient</b>	<b>95% C.I.</b>	<b>t</b>	<b>p</b>
<i>Task stress rating</i>				
Positive emotional style	<b>-0.935*</b>	-1.683 to -0.186	-2.54	0.016
Baseline stress rating	0.022	-0.324 to 0.368	0.13	0.90
Age	0.062	-0.003 to 0.127	1.94	0.061
BMI	0.020	-0.073 to 0.113	0.44	0.66
POMS negative affect	0.065	-0.064 to 0.194	1.02	0.32
<i>Diastolic BP recovery<sup>\$</sup></i>				
Positive emotional style	<b>-3.051*</b>	-5.270 to -0.382	-2.35	0.027
Baseline diastolic BP	-0.045	-0.241 to 0.152	-0.47	0.64
Age	0.002	-0.247 to 0.252	0.019	0.98
BMI	0.198	-0.181 to 0.577	1.08	0.29
POMS negative affect	0.065	-0.417 to 0.546	0.28	0.78
<i>Cortisol post-task<sup>^</sup></i>				
Positive emotional style	<b>-0.408*</b>	-0.741 to -0.075	-2.49	0.018
Baseline cortisol	<b>0.845*</b>	0.528 to 1.162	5.43	0.001
Age	0.007	-0.020 to 0.034	0.53	0.60
BMI	0.001	-0.037 to 0.040	0.08	0.94
POMS negative affect	-0.006	-0.052 to 0.040	-0.26	0.79

\*Significant association (p≤0.05); task stress n=40, \$n=31, ^n=35

### 3.2.3 Hypothesis 3: PES will be associated with faster cortisol recovery

There was a significant main effect of PES group on cortisol responses over time ( $F(1,33)=4.21, p=0.048$ ) and a PES group by time interaction ( $F(1,33)=4.98, p=0.033$ ). The lower PES group demonstrated greater responsiveness to the tasks, illustrated in Figure 3.3. The difference was confirmed in multiple regression on the cortisol value immediately post-tasks, where greater PES was associated with lower cortisol after adjustment for baseline cortisol, age, BMI and negative affect ( $B = -0.408$ , C.I.  $-0.741$  to  $-0.075$ ,  $p=0.018$ ; Table 3.2). PES accounted for 8.4% of the variance in post-task cortisol independently of covariates. The association was weakened after adjusting for CES-D but remained of borderline significance ( $B = -0.339$ , C.I.  $-0.687$  to  $0.008$ ,  $p=0.055$ ). PES was associated with recovery cortisol values in multiple regression, but not after adjusting for negative affect ( $B = -0.303$ , C.I.  $-0.754$  to  $0.147$ ,  $p=0.179$ ). There was no association between POMS vigour and cortisol responses. Of the subjective task ratings, only perceived stress was associated with post-task cortisol values after adjusting for baseline cortisol, age, BMI and negative affect ( $B = 0.183$ , C.I.  $0.033$  to  $0.334$ ,  $p=0.018$ ).

**Figure 3.3 Cortisol release for high and low PES groups**  
Cortisol at baseline, after both tasks and at 20-25 minutes recovery for high PES (solid line) and low PES groups (dotted line), adjusted for age and BMI. Error bars represent standard error of mean ( $n=35$ ).



### 3.3 Discussion

This study showed that higher positive emotional style (PES) derived from mean daily measures of positive mood over seven days was associated with lower subjective stress and greater control during mental stress tasks, accelerated post-stress diastolic BP recovery and reduced cortisol response to stress. These relationships were statistically independent of negative affect or depressive symptoms. A single measure of recalled affect over the past few days, POMS vigour, was associated with diastolic BP recovery but not with subjective task ratings or cortisol responses, indicating a weaker association with psychophysiological stress responses.

The association between positive emotional style and diastolic BP recovery corroborates the previous finding from our group in which EMA-derived happiness predicted diastolic BP recovery from laboratory stressors in a sample of young men (Steptoe et al., 2007a). The effect was substantial, with an additional 16.8% of variance in diastolic BP recovery being accounted for by positive emotional style. Papousek and colleagues (2010) also found that high levels of trait positive affect (measured using the PANAS) were associated with more efficient diastolic but not systolic BP recovery following an exam-style task. These studies suggest a relatively consistent diastolic BP recovery effect from acute mental stress with dispositional positive mood in younger adults. In contrast, psychophysiological stress testing in the Whitehall II cohort of middle-aged adults revealed no association between EMA-assessed positive affect and BP recovery (Steptoe et al., 2005). The Whitehall II study used a Stroop colour-word interference task rather than a socially evaluative speech task. Further studies could investigate whether the nature of the task or the age of the participants have a critical influence on the association between positive affectivity and cardiovascular recovery.

Responses to laboratory mental stress tasks have been shown to be relatively stable and reliable over time (Kamarck et al., 2003). It has been proposed that failure to recover efficiently from acute stress indicates a failure of allostatic regulation (McEwen, 1998a). More rapid blood pressure recovery for those high in positive affect may indicate an adaptive advantage in responding to daily life stressors, which over time, could result in lower risk of hypertension (Stewart and France, 2001) and/or accumulated atherosclerotic damage (Steptoe et al., 2006). Although the literature is limited compared with that on cardiovascular

reactivity, a recent meta-analysis indicated that delayed post-stress BP recovery was associated prospectively with increased cardiovascular disease risk (Chida and Steptoe, 2010).

HPA axis reactivity may also link positive affect to cardiovascular recovery and longer term physical health outcomes (Steptoe et al., 2009). Healthy older adults responding to mental stress tasks with increases in cortisol have been shown to be at significantly higher risk of hypertension (Hamer and Steptoe, 2012) and progression of coronary artery calcification at three years follow-up, after adjustment for conventional risk factors (Hamer et al., 2012). In the current study PES was associated with reduced cortisol stress response independently of covariates. Reduced exposure to cortisol may be one of the mechanisms underlying a reduced risk of cardiovascular disease for individuals with positive emotional traits (Whitworth et al., 2005).

It is notable that associations with biology were stronger for the PES than for POMS mental vigour assessed at the beginning of the laboratory session. Repeated measures of experienced affect over several days may provide a more robust and representative estimate of affective traits than a single evaluative measure (Steptoe et al, 2007). Pressman and Cohen (2005) have argued that measures of affect over multiple time points more reliably predict biological characteristics. Retrospective measures of affect can be strongly influenced by salience memory heuristics, affect infusion effects (Forgas, 1995) and other biases (Miron-Shatz et al., 2009), providing less reliable estimates of experienced affect than those derived from repeated measures.

In the current study, individuals higher in PES reported lower subjective stress during the tasks, perceived them to be less difficult and perceived themselves to be in greater control than in those lower in PES. These effects were independent of negative affect and were unrelated to objective measures of task performance. Importantly PES was not associated with task involvement; engagement-involvement is a fundamental driver of acute psychophysiological responses (Singer, 1974). The evidence suggests that dispositional positive affect is associated with favourable appraisals of acutely stressful circumstances, at least in the laboratory (Tugade et al., 2004). Interestingly neither PES nor subjective task ratings were associated with the magnitude of cardiovascular stress responses. According to



Fredrickson's (2001) broaden-and-build theory, positive emotions 'undo' the physiological arousal affects of negative emotions. Positive emotional experience is thought to be governed in the central nervous system by corticolimbic brain circuitry involving divisions of the cingulate gyrus, the insula and the amygdale (Critchley, 2005). These same areas are responsible for the regulation of cardiovascular and neuroendocrine processes, providing a mechanistic link between affective reports and central regulation of the physiological stress responses. Results from the present study suggest that both cognitive appraisals and subcortical regulatory mechanisms may explain the link between PES and physiological stress responses; PES was related to self-rated task stress and cardiovascular and cortisol stress responses, but subjective stress measures did not explain cardiovascular responses.

The current study was limited by relatively basic measures of task appraisal, so we cannot rule out that differences in more subtle appraisal or adaptive coping mechanisms could help to explain the association between PES and cardiovascular and cortisol stress responses. For example, prolonged negative or ruminative thoughts about a stressor may prolong the physiological response to acute stress (Brosschot and Thayer, 2003). In this small study we were unable to investigate whether PES has physiological correlates that are distinct from related dispositions and personality factors, such as self-esteem (O'Donnell et al., 2008). We endeavoured to statistically control for the effects of depressive symptoms (CES-D) and negative moods (POMS negative affect). However, the limited sample size meant that we did not adjust for both terms simultaneously or other potential confounders such as sleep or socioeconomic status. This study was limited to healthy non-smoking young women with some degree of depressive symptoms and may not generalise to other groups. All exceeded the conventional threshold for moderate to severe psychological distress on the General Health Questionnaire. The mean PES score of the high PES group was only 2.52 on the 0–4 scale, with the highest individual score being 3.36. Levels of positive affect were not therefore extremely high. This factor may distinguish the present study from other investigations of population samples, avoiding possible ceiling effects in the assessment of positive affect.

The present results add to the evidence linking dispositional measures of experienced positive affect with adaptive diastolic BP recovery following acute stress, while extending these results to cortisol. Aggregated repeated measurements of daily positive emotions over

seven days had a more robust association with physiological responses than a single retrospective measure. I identified differences in the perceptions of standardised acute stress tasks for those with higher and lower positive emotional style. The following chapters will investigate the relationships between psychological well-being, perceptions of chronic stressors and biological responses in more detail.

## **Chapter 4 Chronic work stress, heart disease & well-being**

Chapter 3 showed that trait positive emotional style was associated with cognitive, blood pressure and cortisol responses to an acute mental stress task. There has been little attention in the literature reviewed so far towards interactions between psychological well-being and longer term environmental stressors such as work stress, or care-giver stress, and cardiovascular disease. In this chapter, section 4.1 explains why I have focused on work stress as an example of a chronic environmental stressor. I describe alternative definitions for work stress and summarise the evidence linking work stress and heart disease. Section 4.2 provides an overview of the potential mechanisms involved in this association. I review the evidence for the influence of job strain on blood pressure and cortisol in detail since these are pathways which may also be influenced by positive affect, as discussed in the preceding chapters. Section 4.3 outlines potential relationships between positive well-being and work stress in the aetiology of CVD which will be explored in later chapters.

### **4.1 Psychosocial work stress as a risk factor for heart disease**

#### *Why research psychosocial work stress?*

European guidelines for the prevention of cardiovascular disease identify stress at work as a contributory factor to the risks of developing CVD and a poorer prognosis (Perk et al., 2012). Adults of working age spend much of their waking lives at work; on any given full-time working day in 2003 to 2009, non-institutionalised US civilians spent approximately 32% of the day sleeping and approximately 31% at work (Tudor-Locke et al., 2011). Associations between job stress and early atherosclerotic changes have been identified in men in their thirties, indicating that exposure to a stressful work environment has consequences for disease risk from an early age (Kivimaki et al., 2007a).

Estimates of the prevalence of work stress vary depending on the definition of work stress used and the population studied. A 2010 report for the Centers of Disease Control and Prevention in the United States reported that 40% of American workers felt that their job was very or extremely stressful and 25% viewed their job as the number one stressor in their lives

(CDC, 2010). A 2005 survey of over 10,000 UK workers found that 22% were quite or very concerned that stress might cause them harm (Hodgson et al., 2005). A report comparing 27 countries across Europe in 2005 indicated that, on average, 22% of workers experienced stress that they felt had adverse effects their health, with the highest levels in Greece (55%), Slovenia (38%), Sweden (38%) and Latvia (37%)(EU-OSHA, 2009).

In addition to increased risks of heart disease, work stress is also associated with a higher incidence of sleep disruption, psychiatric disorders, musculoskeletal problems and mortality (Stansfeld and Candy, 2006; Knudsen et al., 2007; Chandola, 2010; Nieuwenhuijsen et al., 2010; von Bonsdorff et al., 2012). Lower socioeconomic status is typically associated with a more stressful work environment and stress at work is thought to contribute to the socioeconomic gradient in health (Marmot et al., 1997).

Information overload, intensification of work, 24-hour 'on call' communication and job insecurity in the economic recession may be contributing to workers' perceptions of an increasingly stressful work environment (EU-OSHA, 2012). European Working Conditions Surveys from 1991-2005 show steady growth in the number of respondents who report that they work at very high speed. The annual cost to employers of work-related stress in the UK has been estimated at over £26bn, driven by lost productivity, increased staff turnover and sickness absence (Sainsbury, 2008).

The evidence above suggests that work stress is widely prevalent, costly in terms of health and financial impacts and may be increasing. There is also some evidence from observational studies and natural experiments that specific aspects of work stress are modifiable. For example, Moen et al. (2011) described an organisational intervention to promote greater employee control over work schedules which led to improvements in self-reported sleep, more exercise and greater likelihood of visiting a doctor when sick.

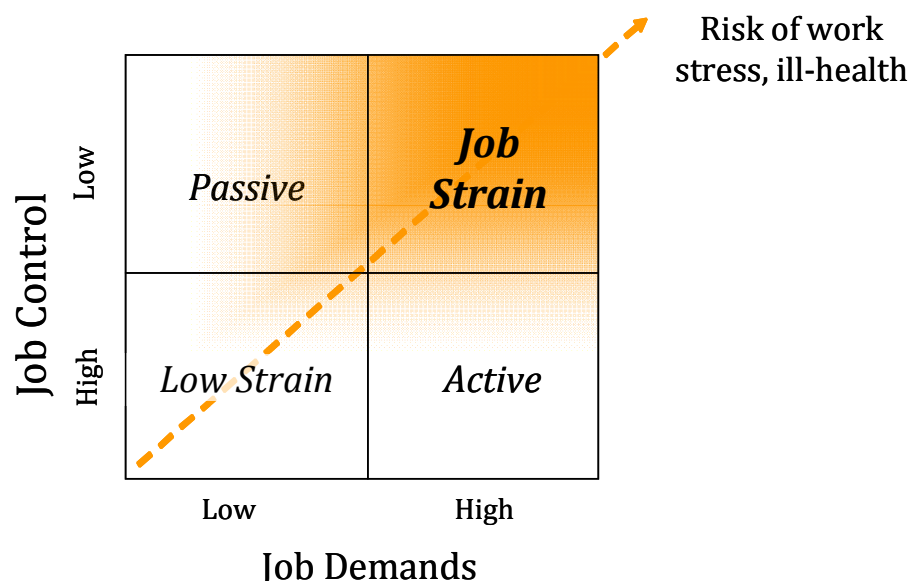
#### **4.1.1 Defining and measuring psychosocial work stress**

*Conceptual models: Job strain, Effort-reward imbalance and Organisational injustice*

Several conceptual models of work stress have been developed which enable a comparison of the consequences of work exposures across different occupations and settings. These models

were developed for work environments where “stressors” are chronic psychosocial influences, not physical or initially life threatening stimuli. The most established and widely studied construct in relation to heart disease is the two-dimensional Demand-Control, or job strain, model (Figure 4.1). Strain is thought to arise when the psychological demands of the job are high (hard and intensive work) and job control is low (control combines measures of task authority and skill discretion) (Karasek, 1979; Karasek and Theorell, 1990). This combination of arousal and restricted opportunities for action or coping with the stressor is thought to lead to the most adverse consequences of physiological strain. If maintained over time, job strain is argued to increase the risk of stress-related illness. The effects of job strain are thought to be most severe in combination with low social support, termed ‘iso-strain’ (Johnson and Hall, 1988).

**Figure 4.1** Job strain arises from a combination of low control and high demands



The effort-reward imbalance (ERI) model was based on principles of co-operative exchange in which stressful conditions arise as a mismatch between the effort exerted and the rewards received (Siegrist, 1996). Siegrist’s definition of effort included both extrinsic environment factors (the demands of the job) and intrinsic personal factors (an ‘overcommitted’ individual coping style). Rewards included esteem (e.g. support, respect), work income and control over status (e.g. job insecurity, promotion prospects).

A third model proposes that a poor perception of justice or fairness at work has an adverse effect on employee health (Elovainio et al., 2002). Ratings of organisational justice, consisting of a procedural component (fair decision-making procedures) and a relational component (fair treatment of individuals), have been found to predict health outcomes independently of the previous models (De Vogli et al., 2007; Kivimaki et al., 2007b).

Other indicators of work stress which have been linked to cardiovascular outcomes include highly vigilant work (Belkic et al., 1998) and job uncertainty, or insecurity (Vahtera et al., 2004). Overtime or excessive working hours have also been linked to cardiovascular outcomes but working time might act as both a physical and a psychosocial stressor (Virtanen et al., 2012). Similarly, shift work is associated with an increased risk of coronary events (Vyas et al., 2012), but this may be due to both psychosocial impacts and the physical effects of routinely waking during the circadian low (Lac and Chamoux, 2004).

#### *Measuring psychosocial work stress*

Standardised questionnaires to assess job strain include the Job Content Questionnaire (JCQ), for which nationally representative data is available in the United States (Karasek et al., 1985); the Swedish Demand-Control Questionnaire (DCQ), which is a reduced version of the JCQ (Theorell et al., 1998) and the Whitehall Job Characteristics Questionnaire, which was adapted for the Whitehall II study of civil servants (Bosma et al., 1997). The Whitehall II study also incorporated questions to assess ERI and to derive a measure of relational organisational justice (Bosma et al., 1997; Ferrie et al., 2006)(Table 4.1). A validation study was recently conducted to derive a measure of job strain, based on similar questionnaire items, which could be applied across 17 European cohort studies (Fransson et al., 2012b).

**Table 4.1 Sample items from scales assessing the three work-stress models**  
adapted from Kivimäki et al. (2006)

Conceptual model	Sample items
Job strain (iso-strain)	Demands: "Do you have to work very fast?" Control: "I have a good deal of say in decisions about work" Support: "When you are having difficulties at work, how often do you get help and support from your colleagues?"
Effort-reward imbalance	Effort: "I am often pressured to work overtime." Rewards: "Considering all my efforts and achievements, I receive the respect and prestige I deserve at work" (reversed)
Organisational justice	"Procedures are designed to hear the concerns of all those affected by the decision" (reversed) "My supervisor treats me fairly" (reversed).

Job strain is usually derived using a quadrant approach by dividing demands and control at the median and selecting those with higher demands and lower control. This leads to an arbitrary cut-off point which differs by population (Kivimäki et al., 2012). Alternative formulations include the quotient approach, in which demands are divided by control, and the subtraction approach (control – demands), which create continuous variables (Courvoisier and Perneger, 2010). There are no definitive guidelines on how to compute a unique job strain score from demands and control subscales, but several large studies have concluded that the impact of job strain is broadly consistent across alternative formulations (Landsbergis et al., 1994; Hintsa et al., 2008).

Self-report questionnaires are inexpensive, easy to administer and allow comparisons between different populations where standardised items are used. Limitations include difficulties due to low literacy, the possibility of self-report bias and problems of validation in different cultures (Landsbergis et al., 2001). An alternative is to impute a mean score for a specific occupation or department, which may be derived from a representative population survey (Johnson and Stewart, 1993). This approach removes self-report bias but loses within-person variability in work characteristics and may also lose time sensitivity. Similar associations between imputed and self-reported job control and first MI were reported in one

comparison study (Theorell et al., 1998). External assessment of job characteristics by external observer or supervisor ratings can also be used to validate self-reports, but this adds an additional layer of cost and complexity (Choi et al., 2008). Objective assessments of workload can be usefully applied to certain occupations to eliminate self-report biases. For example, Virtanen et al. (2008) used monthly records of bed occupancy rates over five years as an objective indicator of work demands in ward staff. The authors were able to demonstrate that ward overcrowding predicted increased rates of antidepressants prescribed for employees, but not vice versa, to show that reverse causality was not the mechanism.

#### **4.1.2 Evidence linking psychosocial work stress to heart disease**

##### *Demand-Control Model*

The association between psychosocial work stress and incident cardiovascular disease has been examined by a number of systematic reviews within the last 10 years (Belkic et al., 2004; Kivimaki et al., 2006; Eller et al., 2009; Backe et al., 2012). The majority of published articles have examined job strain, or its separate dimensions, and CVD outcomes. For example, Backe et al. (2012) reviewed 26 articles (based on 20 cohorts), of which 17 articles examined the association between job strain and incident CVD, including hypertension, and four articles examined the ERI model. A significantly higher risk of CVD was found for workers with high strain relative to low strain in 7/13 cohorts; no studies reported a lower risk.

Kivimaki et al. (2006) applied meta-analytic techniques to derive a quantitative estimate of the magnitude of the risk of incident CHD or cardiovascular mortality associated with work stress. In eleven independent studies that tested the job strain model, an age- and gender- adjusted summary estimate suggested a risk ratio of 1.43 (95% C.I. 1.15 to 1.84). There was some evidence for publication bias but the authors suggested that this was unlikely to have substantially distorted the findings of the meta-analysis. In the largest analysis of prospective individual-level work stress data to date (IPD-Work Consortium), Kivimaki et al. (2012) combined data from 13 independent cohort studies and almost 200,000 participants over a mean of 7.5 years to give an age- and gender- adjusted hazard ratio of 1.23 (95% C.I. 1.10 to 1.37) for incident heart disease. Adjustment for lifestyle factors (BMI, physical activity, smoking, alcohol intake) or conventional cardiovascular risk factors (based on the Framingham score), in addition to socioeconomic status, did not substantially change the



hazard ratio. The IPD-Work Consortium dataset included participants with a broad range of age groups from multiple work sectors and several European countries. Steptoe and Kivimaki (2013) updated the 2006 meta-analysis to include the IPD-Work Consortium data and other studies published up to December 2011. This generated a pooled risk estimate of 1.34 (95% C.I. 1.18 to 1.51) for the effect of job strain on incident CHD and CVD mortality.

Several authors have identified gender differences in the association between work stress and CVD. Systematic reviews by Backe et al. (2012) and Eller et al. (2009) both commented on stronger associations for men and a lack of evidence in female working populations. Notably, a non-significant inverse association between job strain and CVD events was reported in two female cohorts (Lee et al., 2002; Eaker et al., 2004). It has been suggested that for women with a high share of domestic responsibilities, job strain may be less important than the psychosocial burden of the home environment (e.g. childcare). For example, in the Whitehall II cohort, low control at home predicted incident CHD in women but not men (Chandola et al., 2004). In a study examining depressive symptoms as an outcome, job strain only predicted worse outcomes when combined with low social support and a child in the household, as an indicator of home demands (Ertel et al., 2008). The large IPD-Work Consortium analysis reported similar effect sizes in both sexes (Kivimaki et al., 2012), which may suggest that some previous studies were limited by too few cases or a lack of statistical power (Eaker et al., 2004). A recent cohort study in over 20,000 women found similarly increased risks of incident CHD for high strain and active (high demand, high control) jobs compared with low strain jobs (rate ratio 1.38, 95% C.I. 1.1 to 1.8 for both risks) (Slopen et al., 2012).

The iso-strain concept has received less attention than the two-dimensional Demand-Control model. The systematic review by Eller et al. (2009) retrieved seven articles which assessed social support at work, all of which supported an association between lack of support and increased risk of CHD. Three out of three studies which explicitly investigated the presence of iso-strain (job strain and low social support) reported a significant association with incident CHD. Eller et al. (2009) also evaluated studies which looked separately at demands and control. The authors suggested that self-reported demands (but not aggregated measures of demands) more reliably predicted cardiovascular outcomes than job strain, or

control alone. This conclusion was based on only six studies assessing self-report demands. The authors suggested that it would be preferable to report results based on single dimensions rather than the combined dimension of job strain, which is counter to the original model which stated that demands may not be stressful if coupled with sufficient control (Karasek, 1979). The largest study to date found that job strain was a greater risk factor for CVD than either demands or control alone (Kivimaki et al., 2012).

### *Effort-Reward Imbalance*

In the most recent systematic review by Backe et al. (2012), four publications based on three cohorts all reported significant associations between ERI and CVD outcomes in men. For example, in study with the highest study quality, Kuper et al. (2002b) followed up over 10,000 civil servants in the Whitehall II cohort over 11 years and found a 1.26 fold risk of developing incident CHD (95% C.I. 1.03 to 1.55) adjusted for age, sex and traditional risk factors.

The Whitehall II cohort is one of relatively few population studies which have included questions to simultaneously assess ERI and Demand-Control models. In a relatively early study after 5.3 years follow-up, Bosma et al. (1998a) found that ERI predicted a 2.15 fold increased risk of CHD (angina or doctor-diagnosed ischaemia) whereas job strain was only associated with incident disease in men (odds ratio, OR 1.45). In a later analysis with 11 years follow-up, job strain was associated with 1.38 fold increased risk of incident CHD (95% C.I. 1.10 to 1.75) in a model adjusted for age, sex, employment grade and coronary risk factors (Kuper and Marmot, 2003). Peter et al. (2002) compared ERI and job strain as predictors of first MI in a case control study with over 950 cases and 1,000 controls. Controlling each job stress model for the other in order to test the independent effect of either approach did not show systematically increased odds ratios. There was a marginally improved estimation of MI by defining groups exposed to a combination of job strain and ERI, indicating that the models had partly independent associations with incident MI.

### *Organisational justice, job insecurity and other factors*

Eller et al. (2009) identified only two cohort studies which assessed the association between organisational justice and cardiovascular outcomes, both of which reported that greater fairness at work was associated with lower disease risk (Kivimaki et al., 2005; Elovainio et al., 2006). Evidence for job insecurity as a predictor of CVD outcomes was mixed, and the largest

study to date found no evidence of an association (Slopen et al., 2012). In a meta-analysis combining four prospective studies, Virtanen et al. (2012) reported a pooled relative risk of 1.39 (95% C.I. 1.12 to 1.72) for long working hours and risk of CHD. Both overtime work and rotating shift work incorporate both psychosocial and physical exposures, such as prolonged sedentary behaviour or night working, so I do not classify these as exclusively psychosocial work stressors.

Burnout is another work-related factor which has been associated with incident cardiovascular disease (Toker et al., 2012). Burnout is defined as long-term affective state consisting of emotional-exhaustion, physical fatigue and cognitive weariness symptoms (Melamed et al., 1992). Burnout is thought to arise as a result of prolonged exposure to stress at work and is therefore perhaps better characterised as an intermediate health outcome on the pathway to cardiovascular disease, rather than a psychosocial work exposure (Melamed et al., 2006).

#### **4.1.3 Evaluating the evidence: does work stress cause heart disease?**

The majority of prospective studies reviewed above support a causal association between work stress and CHD but the evidence is not entirely consistent and there are some important methodological limitations. Inconsistencies may be partly due to limitations of exposure assessment; work stress may change over time, via a change of job role or a significant alteration in working conditions, yet most studies assess work stress on only one occasion with follow-up years later. Studies in cohorts that used repeated measures to assess changes in job stress found that cumulative stress over time was associated with higher risks of CHD (Chandola et al., 2008), angina in men only (Chandola et al., 2005) and hypertension (Markovitz et al., 2004), which supports a causality argument.

It is difficult to rule out confounding or reverse causation in prospective study designs. Reverse causation, leading to an increased risk of type I error (false positive), could occur if participants with underlying subclinical CHD have increased perceptions of work stress. In the IPD-Work Consortium meta-analysis, Kivimäki et al. (2012) found that the relationship between job strain and incident coronary heart disease was slightly strengthened in models that excluded disease events that occurred in the first five years of follow-up, which the

authors attributed to reduced reverse causation bias. In this analysis, the authors found only subtle age group differences in the effects of job strain. A number of earlier studies reported that associations between CHD and disease outcomes were stronger in younger age groups (Kivimaki et al., 2008; Eller et al., 2009). Non-work related illness and healthy worker participation effects could dilute effects of work stress in older age groups, leading to potential type II error (false null findings). Studies with a longer follow-up duration may also be more likely to lead to misclassification, since workers experiencing stress or ill-health might be more likely to seek early retirement or change jobs, leading to a healthy worker selection effect (Laine et al., 2009).

Confounding could occur if an unmeasured factor accounted for both increased perceptions of job strain and risk of disease. An important potential confounder is pre-employment socioeconomic status, since adverse conditions in childhood might predispose an individual to poorer educational achievement, less favourable working conditions and increased risk of CVD (Marmot et al., 1998). A large Swedish study found that the association between job control and CHD was statistically explained by adverse childhood conditions, but control was imputed and job strain was not reported (Hemmingsson and Lundberg, 2006). Several studies which have statistically adjusted for pre-employment factors, in addition to concurrent socioeconomic status, have found that there is still a residual risk associated with work stress and health outcomes (Elovainio et al., 2007; Westerlund et al., 2012). For example, Hintsa et al. (2010) assessed long-term exposure to job strain across two waves of Whitehall II and measured incident CHD outcomes 8.7 years later. Low job control was a significant predictor of CHD after adjustment for family history of CHD, education, paternal education and social class, number of siblings and height. Adjustment for pre-employment factors changed the associations by only 4.1%.

In recent cohort studies there has been little attention paid to personality factors as potential confounders or effect modifiers. Only one prospective study in the 2006 meta-analysis adjusted for negative affectivity, a factor which could bias perceptions of the work environment as well as being associated with CVD outcomes (Bosma et al., 1998a). A detailed assessment of psychological attributes (hostility, negative affectivity, coping) as potential mediators of the association between job control and CHD by the same authors found that

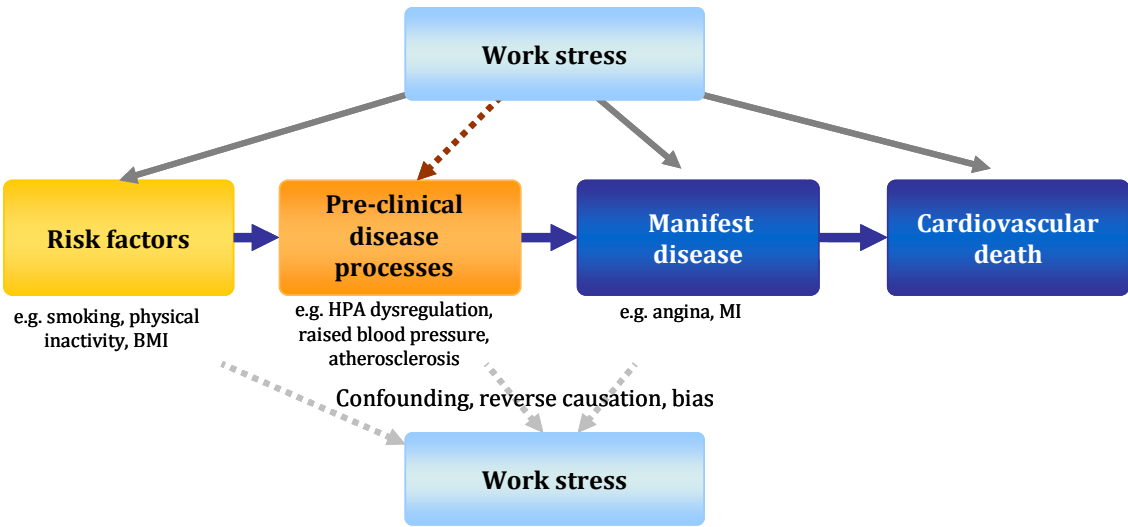
these factors were not confounders, intermediate factors or effect modifiers in the Whitehall II cohort (Bosma et al., 1998b). None of the prospective cohort studies mentioned above made an adjustment for psychological well-being.

Overall, the meta-analysis including over 200,000 workers found that the population attributable risk for job strain and CHD was 3.4%; substantially less than established behavioural risk factors, such as smoking (36%), but could nonetheless account for a notable proportion of CHD deaths, if causal (Kivimaki et al., 2012). Other authors have argued that 3.4% is an underestimate, for example because industrial populations, within whom the association between job strain and health outcomes may be higher, were excluded (Choi et al., 2008; Kivimäki et al., 2012). The precise estimate may depend on the measurement of work stress, the occupational group and length of exposure, but the evidence does support a small but significant independent association between work stress and risk of incident heart disease.

#### 4.2 Mechanisms linking job strain and heart disease

As outlined in section 1.1.2, negative psychosocial factors may influence cardiovascular risk via a number of pathways, but since CVD develops over many years, research has tended to focus on pathways involving lifestyle behaviours and psychobiological pathways influencing pre-clinical disease processes, rather than trigger effects (Figure 4.2).

**Figure 4.2** Pathways from work stress to CVD  
highlighting direct psychobiological mechanisms, adapted from Kivimaki et al. (2006)



### *Behavioural risk factors*

It has been suggested that stressed workers might attempt to self-medicate against stress-induced physiological effects (such as catecholamine secretion) by smoking or drinking (Ayyagari and Sindelar, 2010). Alcohol and cigarettes could also be used to temporarily relieve anxiety or depression associated with job stress. Stress at work may be associated with reduced perceptions of self-control, making it harder to change an unhealthy lifestyle (Muraven and Baumeister, 2000).

Cross-sectional analyses within the IPD-Work Consortium dataset, each based on over 140,000 workers, found that job strain was associated with higher rates of physical inactivity (Fransson et al., 2012a), obese and underweight BMI (Nyberg et al., 2012), smoking (Heikkila et al., 2012b), heavy drinking and abstaining from alcohol (Heikkila et al., 2012a). Individuals with job strain were also more like to report a cluster of four unhealthy lifestyle behaviours (smoking, high BMI, heavy alcohol intake and physical inactivity) and less likely to report no healthy lifestyle factors. However, longitudinal analyses based on over 44,000 individuals followed up for between two and nine years found no association between job strain and change in drinking or smoking behaviours (Heikkila et al., 2012a; b). Both weight gain and weight loss were associated with the onset of job strain during follow-up (Nyberg et al., 2012). In analyses restricted to active participants, the odds of becoming physically inactive were 21% and 20% higher for those with high-strain (OR 1.21, 95% C.I. 1.11 to 1.32) and passive jobs (OR 1.20, 95% C.I. 1.11 to 1.30) at baseline (Fransson et al., 2012a). In the population who reported one to four unhealthy lifestyle factors at baseline (c.75%), the odds of adopting a healthier lifestyle were lower in individuals who had a high strain job at baseline than a low strain job. Job strain did not appear to be associated with drifting into an unhealthy lifestyle in the population with no unhealthy behaviours at baseline. In analysis of the Whitehall II cohort alone, job strain has also been linked prospectively to lower fruit and vegetable consumption (Chandola et al., 2008).

There is therefore some evidence that job strain is associated with an unhealthy lifestyle, but longitudinal associations inconsistent. A monitoring study which assessed both baseline job strain and daily mood and health behaviours over four weeks suggested that proximal within-person daily factors (work hours, positive and negative affect) were more

closely associated with behaviours than iso-strain measures (Jones et al., 2007). Furthermore, the majority of prospective associations between work stress and CHD reviewed in section 4.1.2 above adjusted statistically for health behaviours. For example, Chandola et al. (2008) found that cumulative job strain predicted CHD events after adjustments for smoking, smoking history, diet, physical activity and alcohol consumption. There was a 16% reduction in the hazard ratios when behavioural risk factors were accounted for. The IPD-Work Consortium study reported that adjustment for lifestyle factors (BMI, physical activity, smoking and alcohol intake) did not substantially attenuate the association between job strain and incident CHD (Kivimäki et al., 2012).

#### *Overview of the biological mechanisms linked to work stress*

An overview of the biological pathways thought to link chronic stress and cardiovascular disease processes was given in Chapter 2 (section 2.1). Key mechanisms are thought to include dysregulation of the hypothalamic-pituitary-adrenal axis and autonomic nervous system, and a conversion of temporary increases in blood pressure to permanent hypertension (Brotman et al., 2007; Steptoe and Kivimäki, 2013).

Chandola et al. (2010) conducted a review of sympatho-adrenal and HPA axis biomarkers of workplace stress. They found some evidence for increased levels of urinary catecholamines, lower heart rate variability, a greater cortisol awakening response, higher levels of prolactin and lower levels of testosterone. The authors commented that the findings were not consistent and the majority of studies were cross-sectional and based on small samples. The largest cross-sectional study to examine job strain and biomarkers to date, based on 47,000 individuals from the IPD-Work Consortium, found an association between job strain and diabetes, but no association with clinic blood pressure or blood lipids (Nyberg et al., 2013). One of the few prospective studies found an association cumulative job strain and risk of metabolic syndrome after approximately six years and low heart rate variability another 10 years later in the Whitehall II cohort (Chandola et al., 2008). The components of metabolic syndrome included in this study were raised waist circumference, raised serum triglycerides, raised total cholesterol, low high density lipoprotein cholesterol, raised systolic blood pressure or antihypertensive medication and raised fasting glucose. Metabolic syndrome accounted for approximately 16% of the increased risk of CHD associated with job strain, independent of health behaviours.

Metabolic syndrome is known to be associated with a pro-inflammatory state (Hotamisligil, 2006) and several studies have reported an association between ERI and increased acute inflammatory responses to laboratory stress tasks (Hamer et al., 2006; Bellingrath et al., 2010; 2013). In a cross-sectional study in over 950 workers, Emery et al. (2012) found that job strain was associated with increased C-reactive protein, but this association was explained by lower physical activity in stressed workers. Bellingrath et al. (2013) showed that teachers experiencing high ERI had reduced anti-inflammatory regulatory capacity by glucocorticoids. This was assessed via an in vitro test of suppression of IL-6 in response to dexamethasone, an anti-inflammatory agent.

There is some evidence that work stress is associated with atherosclerosis, and may be associated with its progression. The Young Finns study assessed biological, familial and socioeconomic risk factors for CHD at 12 to 18 years of age and job strain and carotid artery intima-media thickness (IMT) at 33 to 39 years of age in 358 men. In cross-sectional analysis in 2001, higher job strain predicted greater IMT in men, an effect which was not attenuated after adjustment for pre-employment factors (Kivimaki et al., 2007a). However, no cross-sectional association between job strain and IMT was found in the same cohort six years later (Rosenstrom et al., 2011). From 2001 to 2007 there was no linear association between job strain and IMT progression but large decreases in job strain were associated with slower progression of IMT. Combined decreases in demands and control (a shift towards passive jobs) were associated with greater IMT progression. Fujishiro et al. (2011) found no association between carotid IMT and job strain or demands in a study of over 3000 working adults but low control and blue-collar jobs were associated with carotid IMT. Job stress exposures were assessed two years after IMT measurement, increasing the risk of misclassification.

Variation in individual susceptibilities and exposures may explain inconsistent associations between work stress and biological outcomes, especially in smaller samples. Laboratory-based psychophysiological stress studies have been used to investigate how job strain and workplace biomarkers relate to individual patterns of stress reactivity. In a meta-analysis of 20 studies which used various measures of chronic job stress as psychosocial predictors, Chida and Hamer (2008) did not find a statistically significant association with



stress reactivity or recovery, but the meta-analysis did not differentiate between different types of acute stressor. Steptoe et al. (1993) showed in a small study of 40 older men that individuals randomised to an uncontrollable (externally paced) task had higher BP and heart rate reactivity than those who completed a controllable (self-paced task). The combination of chronic job strain and with allocation to the uncontrollable task was associated with the most pronounced cardiovascular reactivity, a finding that was later repeated in a larger study of 162 teachers (Steptoe et al., 1999). Importantly, in one study of firefighters, the combination of job strain and high acute stress reactivity in the lab predicted higher ABP at work, whereas job strain or stress reactivity alone were not significantly associated with ABP (Steptoe et al., 1995). In an older population of 591 working men aged 42-60 years, Everson et al. (1997) found an interaction between stress reactivity and work demands, so that men with a combination of high work demands and large systolic blood pressure increases in anticipation of an exercise test had 10-40% greater progression of carotid IMT than men with lower reactivity and low demands. Individual differences in stress reactivity may be influenced by early life experiences: Westerlund et al. (2012) showed that an index of social adversity in adolescence interacted with job strain at age 43 to predict biological stress. Job strain was only associated with increased allostatic load (a summary measure of body fat, blood pressure, inflammatory markers, glucose, blood lipids and cortisol) in participants with a history of childhood social adversity.

In summary, there is evidence linking work stress to 'upstream' markers of HPA axis and autonomic nervous system regulation, secondary inflammatory mediators, the metabolic syndrome and atherosclerotic processes, but associations may be influenced by interactions between individual sensitivities and changing environmental exposures.

In the next section I review the evidence in more detail for two key biological markers implicated in the processes linking work stress to CHD: blood pressure and cortisol. As discussed in the preceding chapters, these factors have also been associated with psychological well-being. The following review will assess the strength of the evidence from observational studies linking job strain to blood pressure (4.2.1) and salivary cortisol (4.2.2), and whether any association is independent of psychological well-being. I focus on studies which have used job strain as the work stress exposure, since this is the model for which the

most evidence is available. ERI, organisational justice and job strain appear to have effects on CHD outcomes which are partially independent, so it is possible that there may be slight differences in their associations with biological markers (Maina et al., 2009a).

#### **4.2.1 Job strain and blood pressure**

A recent narrative review of the association between occupational stress and hypertension referred to 'vast evidence' linking job strain and blood pressure elevation (Rosenthal and Alter, 2012). It has been shown that individual blood pressure is higher by an estimated four millimetres of mercury (mmHg) at work than outside work (Schwartz et al., 1994). Blood pressure is lower on leisure days than work days (Pieper et al., 1993). It was unclear from studies using casual clinic measures of blood pressure whether psychosocial work characteristics accounted for these differences (Schnall et al., 1994). In a recent systematic review, Landsbergis et al. (2013) conducted a meta-analysis of 22 cross-sectional studies based on ambulatory blood pressure (ABP) monitoring and found that job strain was associated with elevated work systolic BP (+3.4 mmHg, 95% C.I. 2.0 to 4.8) and diastolic BP (+2.1 mmHg, 95% C.I. 1.2 to 3.0), after adjusting for hypertension risk factors. Job strain also predicted home and sleep BP, but not 24-hour ABP (based on only 9 studies). Effects were stronger for men, but none of the gender interaction terms were significant.

Research to assess the relationship between job strain and blood pressure is subject to many of the same limitations, such as risks of confounding and bias, as literature assessing CVD outcomes, but the measurement of blood pressure offers an additional complication. As explained in section 2.2.2, casual clinic measures are thought to be prone to observer error, 'white coat' effect and the inherent variability of blood pressure. ABP measures have the advantage of repeated measures and ecological validity. They may therefore be more sensitive to psychosocial and environmental factors (Carels, 1998). Interpretation of ambulatory data can also be complicated by physical activity; one study found that associations between job strain and ABP were improved by excluding participants with physically demanding jobs (Theorell et al., 1991).

If job strain has a causal influence on elevated blood pressure, longitudinal studies would be expected to show an increased risk over time associated with cumulative exposure.

The review by Landsbergis et al. (2013) identified five longitudinal studies which assessed job strain and ABP changes over time, of which three offered at least partial support for a causal hypothesis. One study assessed strain and ABP in 73 workers four times over one year (Theorell et al., 1988). Time periods with the highest strain were associated with higher work systolic BP. Tobe et al. (2005) reported a trend for job strain to predict increased ABP in 115 middle-aged men one year later, but no association in 148 women. Riese et al. (2000) found no influence of change in job strain on ABP in 159 female nurses. Fauvel and colleagues reported that job strain predicted work ABP in 292 chemical workers at baseline, but they found no association with job strain, or change in job strain, and incident hypertension five years later (Fauvel et al., 2001; Fauvel et al., 2003). None of these studies factored in individual differences in stress reactivity. Steptoe et al. (2000b) demonstrated that the combination of high stress reactivity to an uncontrollable lab task and persistently high job demands over one year predicted raised systolic and diastolic BP over a working day.

The most compelling evidence for a longitudinal association between job strain and ABP to date involved 195 men working across eight New York work sites who completed a job strain questionnaire and 24-hour ABP at baseline and three years later (Schnall et al., 1998). There was a cross-sectional association between job strain and higher ABP at both time points, but men with job strain at both time-points had work systolic/diastolic ABP that was +11/+7mmHg higher than those without job strain. Importantly, men with job strain at baseline but not at follow-up reported a decrease in work and home ABP (-5.3/-3.2 mmHg), indicating that changes in blood pressure related to job strain may be temporary and reversible following improvements to the work environment.

These longitudinal ABP findings were reinforced by a larger study of 8395 white-collar workers employed by public organisations with clinic BP measures followed-up over 7.5 years (Guimont et al., 2006). Compared with men who had never reported job strain, men with cumulative exposure and exposed during follow-up had increased systolic (+1.8 mmHg, 95% C.I. 0.1 to 3.5) and diastolic BP (+1.5 mmHg, 95% C.I. 0.2 to 2.8). Effects were smaller in women. Concordant with the iso-strain model, effects were larger in workers with low levels of social support at work. Although the study relied on a clinic assessment of BP, the strengths

of the study included a wide range of ages and occupations, low loss to follow-up (10%, vs. 46% for Fauvel et al.) and use of the standardised Job Content Questionnaire.

Blood pressure is thought to increase the risk of cardiovascular disease in a linear fashion, so even small elevations in blood pressure associated with job strain may contribute to cardiovascular risk (Kshirsagar et al., 2006). In addition to the study by Fauvel et al. (2003) described above, two longitudinal studies have assessed hypertension as an outcome, a condition defined as sustained blood pressure above 140/90mmHg. Markovitz et al. (2004) found that an increase in job strain over 8 years predicted incident hypertension (or hypertensive medication) in 3,200 employed adults, aged 20 to 32 at baseline. In direct contradiction, in the Whitehall II study of over 8,000 civil servants, there was no association between job strain and incident hypertension. Although both job strain and hypertension predicted incident CHD, the effects were independent of one another (Kivimäki et al., 2007). The authors concluded that the development of hypertension is not the primary cause of CHD in employees with job strain. However, this study was limited by the use of casual clinic BP measured outside the work environment.

In summary, there is relatively strong evidence from ambulatory studies that job strain is associated with transient increases in blood pressure during working days but evidence for cumulative effects over time is less consistent. Outcomes are likely to be influenced by the duration and type of work exposures in addition to intrinsic differences in stress reactivity. Small elevations in blood pressure on work days could increase sheer stress and promote atherosclerotic processes in susceptible individuals (Folkow, 1982). Acute blood pressure elevations could also act as a trigger for rupture of atherosclerotic plaques, leading to coronary events in employees with prevalent CHD (Strike and Steptoe, 2005). I identified only one study which measured job strain, positive affect and ABP: Theorell et al. (1993) recruited 56 healthy female nurses aged 20 to 59 to complete hourly measurements of BP and mood ratings over both work and leisure time over one day. Higher happiness predicted lower BP during work and leisure time whereas job strain predicted higher BP readings at work only. The effects of happiness and job strain were largely independent.

#### **4.2.2 Job strain and salivary cortisol**

As outlined in Chapter 2, three distinct measures of the diurnal rhythm of cortisol are frequently used as indicators of HPA axis functioning: the response to awakening (CAR), the steepness of the decline from morning to evening and the total or mean daily output. In a systematic review and meta-analysis, Chida and Steptoe (2009b) found that job stress was positively associated with the size of the CARi, the increase on waking ( $r=0.061$ , 95% C.I. 0.012 to 0.110). Although 22 different work stress exposures were included in this meta-analysis, findings were drawn from only eight articles, each of which measured multiple work stress exposures within a single cohort (eight cohorts in total). The results were not split out by work stress model, but the authors did note that the result was robust when limited to higher quality studies.

In their narrative review of work stress biomarkers, Chandola et al. (2010) identified 16 studies which measured post-morning or diurnal cortisol rhythm using saliva samples of which six identified positive associations, four negative associations and nine found no significant association. Similarly conflicting results were reported in a review of work stress studies investigating cortisol in blood and urine by Hansen et al. (2009) which found nine positive associations, three negative and 11 non-significant results. Hansen and colleagues acknowledged that blood or urine sampling schedules may have failed to take into account the diurnal rhythm of cortisol, and therefore may not have been sensitive to psychosocial influences. Chandola et al. (2010) did not evaluate sampling schedule, study quality or discuss results by work exposure.

Weaknesses in study design might explain the conflicting associations. As discussed in section 2.2.3, a large number of factors can influence the diurnal cortisol rhythm, including waking time, work or leisure days, medication use, menstrual timing, caffeine intake, smoking, sleep duration and quality (Adam and Kumari, 2009; Kumari et al., 2009). Shift work and especially night work disrupts the normal endogenous sleep/wake cycle and is known to disrupt the circadian rhythm (Scheer et al., 2009). Any studies examining the influences of work stress on cortisol in occupations involved in shift work should therefore standardise or specify type of shift.

Specific types of psychosocial work stress exposure may be particularly important for cortisol. Frankenhaeuser (1989) suggested that although demanding conditions stimulate a catecholamine response, cortisol will only increase in a low control (high strain) situation. Empirical support for this hypothesis was reported by Hausser et al. (2011) who measured cortisol in 77 men and women completing manipulated work stress tasks. High workload (demands) was only associated with increased cortisol in a machine-paced task (low control), not in a self-paced task (high control). In a comparison between the ERI model and the job strain as predictors of the cortisol awakening response in 104 call centre operators, Maina et al. (2009a) found that job strain was positively associated with the awakening response but ERI had a negative association. The meta-analysis by Chida and Steptoe (2009) found that although work stress predicted an increased awakening response, measures of burnout, fatigue and exhaustion were associated with a reduced CAR (Chida and Steptoe, 2009b).

I conducted a systematic review of the literature to identify studies which assessed the relationship between job strain, or separate components of the demand-control model, and the diurnal rhythm of salivary cortisol. I aimed to investigate whether the apparently inconsistent results identified in reviews by Chandola (2010) and Hansen (2009) could be resolved by concentrating on a single model of work stress exposure and specific salivary cortisol indicators: the increase on awakening, diurnal slope and total output over the day.

### *Search strategy*

I conducted a keyword search for studies investigating job strain, job demands, job control or iso-strain and salivary cortisol in PubMed and PsycInfo.<sup>11</sup> The search retrieved n=44 articles in PubMed and an additional n=9 articles in PsychInfo. Five additional articles were retrieved through searching the references of relevant articles. Abstracts were screened for the following criteria: i) original empirical study, ii) constructs from the job strain model assessed as an exposure (strain, demands, control, support at work, iso-strain), iii) outcomes to include the CAR/diurnal slope/total daily output assessed with salivary cortisol, iv) full text English language article available, v) peer-reviewed journal article. Studies which assessed morning or day-time salivary cortisol based on a single time-point during the day were not included.

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<sup>11</sup> Search terms: ("job strain" OR "job control" OR "job demands" OR "iso-strain") AND cortisol, retrieved 53 articles 20<sup>th</sup> Feb 2013, excluding duplicates

In order to compare methodological quality, I constructed a simple quality rating based on study protocol and sample size. Studies scored one point for positive attributes and zero if the attribute was not present, or not mentioned, up to a maximum 10 out of 10. Positive attributes were: i) n=200+ participants (larger statistical power); ii) 2+ days of sampling (to increase within-person reliability); iii) specified work and/or rest day; iv) samples timed from waking; v) shift workers excluded or shift work standardised; vi) exclusion of samples outside timed protocol; confounders considered included vii) time of waking, viii) socioeconomic status, ix) sleep and/or health behaviours; x) longitudinal study with multiple assessments of exposure and/or cortisol. Single occupation studies (nurses, teachers) arguably did not need to control for socioeconomic status, and were allocated this point. I was also interested in whether positive affect was measured within the study and any noted association with job strain or cortisol. Only studies which applied the Karasek job strain model to assess work stress were included in the review but other work stress exposures examined within the same study were noted.

#### *Literature review findings*

Of the 58 papers retrieved, 42 were excluded for following reasons: n=6 review paper, n=6 association between job strain and cortisol not assessed, n=17 no relevant salivary cortisol outcome, n=6 results duplicated another paper based on the same cohort, n=4 experimental studies, n=2 no full text available, n=1 dissertation. The remaining 17 articles were grouped by cortisol outcome and listed in Table 4.2 a)-c): n=11 articles assessed the CAR (a); n=8 the diurnal decline (b); n=6 a measure of output over the day (c). Studies which used a single cortisol sample to indicate 'morning' or waking cortisol, rather than measuring the awakening response, were not included as measures of the CAR (Steptoe et al., 2000a; Rystedt et al., 2008). Studies are ranked in order of quality score.

#### *a) Cortisol awakening response, Table 4.2a)*

There was no consistent pattern identified between work exposures associated with job strain and the CAR. Six articles provided partial support for an association between job strain and a higher CAR reported in the meta-analysis by Chida and Steptoe (2009b), n=3 articles reported no association and n=2 articles suggested strain was associated with a lower CAR.

The studies reporting a positive association each reported important caveats: Maina et al. (2009a) reported that job strain predicted a higher area under the curve relative to zero, or ground (CARaucg) in the first hour after waking, but no association with the mean increase on awakening (CARi) or the area under the curve with respect to increase (CARauci)(Pruessner et al., 2003). Furthermore, the significant association was found in only one of two call centres. Chandola et al. (2008) reported a positive cross-sectional association between iso-strain and the CARi in over 3,700 civil servants, but no association with cumulative iso-strain assessed 12-15 years earlier. Hibel et al. (2012) and Kunz-Ebrecht et al. (2004b) found no direct associations; strain or high demands interacted with an additional psychosocial stressor (parenting stress or low socioeconomic status) to produce a higher CAR. Alderling et al. (2006) found that lower strain was associated with a lower CAR in women only; Karlson et al. (2011) reported that low control was associated with a higher CAR in men and women, but low demands also predicted a higher CAR in men.

A third study which reported different effects by gender found that social support at work, which is conceptually associated with lower strain, was associated with a higher CAR in men only: Holleman et al. (2012) reported in a study of almost 2000 Dutch adults that while strain had no direct effect on the CARauci, there was an interaction with history of childhood trauma such that trauma and greater demands or lower control were associated with a lower CARauci.

Studies with higher quality scores found both positive and null findings. All included studies measured the CAR from time of waking. The two largest population studies reported opposing findings, but both relied on only one day of sampling (Chandola et al., 2008; Holleman et al., 2012). Only four studies used multiple sampling days and these reported both positive and null associations with strain. Only two studies specified that participants were day shift workers (Harris et al., 2007; Maina et al., 2009b). No studies reported repeated assessments of the CAR over time and the only study to investigate cumulative job strain found no association with the CAR (Chandola et al., 2008).

#### *b) Diurnal slope, or evening level*

Four out of five studies assessing the evening level of cortisol as an indicator of the diurnal decline found that exposures associated with greater strain were associated with higher



evening levels (Fox et al., 1993; Sjogren et al., 2006; Harris et al., 2007; Rystedt et al., 2008). These studies all measured cortisol over several working days. The significant exposure predictors varied by study, including low control only, high objective demands, high subjective strain and iso-strain. The only longitudinal design was described by Rystedt et al. (2008) who classified participants with chronic iso-strain based on three questionnaires completed over 3.5 years. Chronic iso-strain predicted higher evening cortisol on both weekend and work days. A conflicting association was reported by Holleman et al. (2012), who found that childhood trauma interacted with high job control to give higher evening cortisol levels. The majority of adults in this study had a remitted depressive disorder and sampling was conducted only on one day (work or rest day not specified), so results may not generalise to healthy populations.

Of the five studies assessing diurnal decline, n=3 studies found no association with job strain (Steptoe et al., 2000a; Sjogren et al., 2006; Harris et al., 2007), n=1 a greater decline (Steptoe et al., 2000a) and n=1 a flatter rhythm, or less decline (Karlson et al., 2011). It is difficult to compare these studies since the 'diurnal decline' was assessed in five different ways; for example, the difference between morning peak and 10pm levels (Harris et al., 2007), difference between bedtime and waking sample (Sjogren et al., 2006) or the difference between 10pm and 8am samples, not based on time of waking (Steptoe et al., 2000a).

### *c) Output over the day*

Five out of six studies found no significant association between measures of exposure to strain at work and mean cortisol output over the day. The one exception was the study by Kunz-Ebrecht et al. (2004b), which treated demands and control exposures separately. In men, high job control predicted lower cortisol throughout the day, whereas in women, high demands predicted higher output only in women with lower socioeconomic status.

**Table 4.2 Associations between psychosocial job strain and cortisol a) the CAR**

First author (date)	Population, n	Work stress exposure(s)	Sampling day(s)	Procedure	From time of waking	Shift	Non-comp.	Covariates	Significant association(s) with CAR	No significant association(s) with CAR	Support for strain and higher CAR?	Quality score (/10)
Maina (2009)	n=104 workers from 2 call centers (28 M, 76 W)	Strain (=quadrant term, 4 categories), demands, ERI (effort/reward as binary <=1 vs >1), overcommitment	3: 2 work, 1 leisure	7 samples: waking, +30m, +60m, start of work shift, +every 3h <i>AUCg, AUCi, CARi based on first hour after waking. exc. &lt;2.5nmol/l CARi</i>	Yes	day	Yes	age, gender, education level, marital status, waking time, sleep duration, sleep quality, weekdays, work schedule, adherence	AUCg: strain (+) in one centre only; effort (-) in one centre, reward (+) in one centre, ERI (-) in one centre	No measures associated with CARi or AUCi AUCg not associated with demands or control assessed separately	(+ve) one centre / (null) one centre	8
Chandola (2008)	n=c.3,700 civil servant Whitehall II participants, with cortisol data	Iso-strain, cumulative measure of strain reported in '85-88, '89-90 or '02-04 (0-2)	1 day	2 samples: waking, waking +30m ( <i>CARi</i> ) assessed at phase 7 '02-04	Yes	*	Yes	age, gender, employment grade, waking time, hypertension, total cholesterol, smoking, health behaviours	Cross-sectional association, iso-strain (+) higher CAR	Cumulative iso-strain measured up to 12 years earlier had no association with CARi	(+ve) cross-sectional only	7
Hibel (2012)	n=56 US working mothers with children aged 2-4	Strain (=demands/control & skill discretion), demands, control	4: 2 rest days, 2 work days	2 samples per day: waking and waking +30m to calculate <i>CARi</i>	Yes	*	Yes	age, income, waking time, sleeping time, bed time, medication use, sample delay, health status, marital status, smoking	No direct effect of strain on <i>CARi</i> <i>Interaction: higher parenting stress plus strain associated with higher CAR on work days</i>	Strain only, demands, control	(+ve) interaction only	7
Harris (2007)	n=28 nursing home staff, all women (with data for first 3 samples)	Demands, control (decision latitude & authority), support at work, ERI	2 consecutive work days	5 samples over 2 days: waking, +30m, +45m, 1500, 2200 <i>CARauc based on first 3 samples</i>	Yes	day	Yes	age, vitality, physical functioning, general health, coping, tobacco, BMI, coffee	No direct effect of control or demands on <i>CARauc</i> <i>Correlations: higher control with lower CARauc, social support at work with higher CARauc, but not sig. after adjusting for covariates</i>	Demands, ERI	(null)	7
Sjogren (2006)	n=193 Swedish working adults, population survey	Demands, control, support at work	3 consecutive working days	3 samples: waking, +30m, before going to bed ( <i>CARi</i> )	Yes	*	Yes	age, gender, time of waking, regular medication, smoking, alcohol	No direct effects <i>Interaction between CAR, gender and control &amp; CAR, gender and support at work, but no sig. effects in stratified analyses, direction of interactions not reported</i>	Demands, control, support at work	(null)	6
Kunz-Ebrecht (2004)	n=181 UK Whitehall II cohort, (97M, 84W); high SES n=126 vs. low SES n=55	Demands, control (not strain)	1 work day	10 samples: waking, waking +30m, 8 2-hourly 30 minute intervals until 2200-2230 <i>CARi first 2 samples</i>	Yes	*	Yes	age, ses, time of waking, smoking	Interaction between SES and job demands, with higher CAR in low SES participants reporting high demands (+)	Control	(+ve) interaction only	6

**Table 4.2 Associations between psychosocial job strain and a) the CAR (continued)**

First author (date)	Population, n	Work stress exposure(s)	Sampling day(s)	Procedure	From time of waking	Shift	Non-comp.	Covariates	Significant association(s) with CAR	No significant association(s) with CAR	Support for strain and higher CAR?	Quality score (/10)
Holleman (2012)	n=1995 Dutch adults working >8h/week, 76% had remitted anxiety/depressive disorder (65% W)	Strain (=quadrant term, strain vs. other & quotient d/c), demands, control, support at work	1 day (63% work day)	7 samples: waking, +30/45/60m, 2200, 2300 <i>AUCg and AUCi based on first hour after waking.</i> DST also conducted	Yes	*	*	age, gender, education, work/rest day, time of waking, sleep, daylight, CVD, depressive or anxiety disorders, physical activity, smoking	No direct effect of strain on CARauc <i>Childhood trauma*work stress interaction, history of trauma associated with lower cortisol when reporting high demands, higher cortisol with control or support at work</i>	Strain, demands, control, support at work only <i>In DST, low social support at work &amp; high job strain predict more cortisol suppression after DST</i>	(-ve) interaction only	5
Alderling (2006)	n=529, employed adults from a Swedish population study (348 W, 181 M)	Strain (median split to 4 groups)	1 work day	4 samples: waking, +30m, at lunch, before bed <i>CARi based on first 2 samples</i>	Yes	*	Y	age, gender, medication use, part-time work, life events, depression, well-being, obesity, smoking, alcohol ( <i>no confounding effects</i> )	<i>No effect of high strain vs. low strain on CARi; peak levels lower in women with low strain than high strain, active or passive</i>	M: strain, demands, control W: demands, control	(null) / (+ve) for women only	5
Karlson (2011)	n=383 employees across different sectors (257f, 126m)	Strain, demands, control, ERI, overcommitment	1 work day	4 samples: waking, waking +45m, waking +8hr, 2100 <i>CARi based on waking and +45m, dichotomised highest quartile vs. rest</i>	Yes	*	No	age, waking time, antidepressant medication	Low job control associated with higher CARi <i>Interaction with gender, M: low demands associated with higher CARi (no association for women)</i>	Support at work, effort, reward, ERI, overcommitment	(+ve) low control only, opposite direction effect with demands in men	4
Eller (2006)	n=83 Danish working adults (28 M, 58 W)	Strain, demands, control, support at work, ERI, effort, reward, time pressure (split at mean)	1 day	6 samples: waking, +20m, +30m, + 60m, +8h, 1800 <i>CAR=S1 &amp; S3, repeated measures analysis</i>	Yes	*	*	age, time of first sample, physical activity, smoking	M: high social support at work, higher CAR <i>Feeling of time pressure and ERI associated with higher CARi (+)</i>	Strain, demands, control	(null)/(-ve) effect, based on support at work for men only	3
Wright (2008)	n=98 Australian adult training and support workers (43 M, 55 W), working >30h/w	Strain (quadrant term, 4 categories & quotient d/c)	1 day	2 samples: waking, waking +30m ( <i>CARi</i> )	Yes	*	*		No direct effect of strain on CARi <i>Combination of demands, control and support at work explained more of variance in CARi than individual terms</i>	Quadrant and quotient strain, demands, control	(null)	1

Column headings: 'From time of waking'=samples anchored on waking time, yes/no; 'Shift'=study specified whether participants worked only during the day or rotating/night shifts, \*=not specified; 'Non-comp.'=measures taken to exclude non-compliant participants or samples, e.g. samples >10m outside timed protocol; 'Support for strain and higher CAR?=does this study support an association between higher job strain and a heightened CAR? (Chida and Steptoe 2009); 'Quality score'=rating of study methodology, described in main text

M=men;W=women; SES=socioeconomic status; CARi=cortisol increase on awakening, difference between peak and waking level; CARauc=cortisol area under the curve, based on morning samples only

**Table 4.2 Associations between psychosocial job strain and b) the diurnal decline**

First author (date)	Population, n	Work stress exposure(s)	Sampling day(s)	Procedure	Time of waking	Shift	Non-comp.	Covariates considered	Significant association(s) with diurnal decline	No significant association(s) with diurnal decline	Support for strain model and flatter DD/higher pm level?	Quality score (/10)
Harris (2007)	n=40 women, nursing home staff (with evening data)	Demands, control, social support at work, ERI	2 consecutive work days	5 samples over 2 days: wake-up, +30m, +45m, 1500, 2200 <i>DD=difference between 2200 sample and wake-up+45m</i>	Yes	day	Yes	age, vitality, physical functioning, general health, coping, tobacco, BMI, coffee	<b>2200h:</b> low control (decision authority) associated with higher evening cortisol	<b>DD:</b> demands, support at work, ERI <b>2200:</b> demands, support at work, ERI <i>coffee also sig predicts evening cortisol (+)</i>	<b>DD:</b> (null) <b>pm:</b> (+ve) for control only	7
Sjogren (2006)	n=193 Swedish working adults, population survey	Demands, control, support at work	3 consecutive working days	3 samples: waking, +30m, before going to bed <i>DD= difference between bedtime and waking sample</i>	Yes	*	Yes	age, gender, time of waking, regular medication, smoking, alcohol	<b>Bedtime:</b> high demands, high control (decision latitude) and low social support at work associated with higher evening cortisol	<b>DD:</b> demands, control, social support at work (in adjusted analyses)	<b>DD:</b> (null) <b>pm:</b> (+ve) demands, support at work; (-ve) control	6
Fox (1993)	n=151 US nurses (all W)	Demands (objective and subjective measures), control, strain (demands* control interaction term)	2 work days	3 samples over a day: waking, 2-3h after starting work, 2-3h after return from work in evening <i>Evening home measure used as pm reading</i>	Yes	day	*	age, body weight, daily caffeine consumption	i) objective demands (percentage patient contact) associated with higher post-work cortisol; ii) subjective demands predict high cortisol at work only with low control	No associations with control only	<b>pm:</b> (+ve) demands, strain	6
Rystedt (2008)	n=77, white collar workers, (52M, 24 W)	Iso-strain based on 3 questionnaires over 3.5 years, split at median into high n=38 vs. low n=39 iso-strain	7 consecutive days	2 samples per day over 7 days: waking and 10pm <i>MANCOVA analysis with iso-strain and weekday/weekend as independent variables</i>	Yes	day	*	age, gender, work day/weekend	<b>2200:</b> chronic iso-strain positively associated with evening cortisol on work and rest days		<b>pm:</b> (+ve) iso-strain	5

**Table 4.2 Associations between psychosocial job strain and b) the diurnal decline (continued)**

First author (date)	Population, n	Work stress exposure(s)	Sampling day(s)	Procedure	Time of waking	Shift	Non-comp.	Covariates considered	Significant association(s) with diurnal decline	No significant association(s) with diurnal decline	Support for strain model and flatter DD/higher pm level?	Quality score (/10)
Holleman (2012)	n=1995 Dutch adults working >8h/week, 76% had remitted anxiety/depressive disorder (65% W)	Strain (=quadrant term, strain vs. other & quotient d/c), demands, control, support at work	1 day	7 samples: wake-up, +30/45/60m, 2200, 2300 <i>Examined evening value, mean 2200 and 2300</i>	Yes	day	*	age, gender, education, work/rest day, time of waking, sleep, daylight, CVD, depressive or anxiety disorders, physical activity, smoking	No direct effects <i>Interaction with job control - higher evening values with greater job control at work and childhood trauma</i>	<b>2230:</b> strain, demands, control, support at work	<b>pm:</b> (-ve) interaction with control only	5
Thomas (2009)	n=7916 working adults aged 45 years, 1958 British birth cohort	Strain (=quadrant term, strain vs. other) <i>Also overtime work, regular night work</i>	1 day	2 samples: waking +45m, waking +3h45 <i>DD= difference between two samples over 3h</i>	Yes	identified night workers	No	ses at birth, education, adult ses, marital status, night work, smoking		<b>DD:</b> Strain, overtime, night work	<b>DD:</b> (null) <i>but morning decline only</i>	5
Karlson (2011)	n=383 Swedish employees across different sectors (126 M, 257 W)	Strain, demands, control, ERI, overcommitment	1 work day	4 samples: waking, waking +45m, waking +8h, 2100 <i>DD= difference between 2100 and peak am sample, dichotomised highest quartile vs. rest</i>	Yes	*	No	age, gender, waking time, antidepressant medication	<b>DD:</b> high demands associated with less decline <i>Gender interaction - steeper declines associated with high rewards, ERI, opposite in men</i>	<b>DD:</b> strain, control, support at work	<b>DD:</b> (+ve) demands only	4
Steptoe (2000)	n=105 UK teachers with high or low job strain scores, defined 12months prior	Strain (=demands/control; high d>c vs low d<c), demands, control, skill utilisation	1 work day	8 samples at 2hr intervals from 0800-0830 to 2200-2230, first sample taken on arrival at school <i>DD= difference between 0800 and 2200 sample</i>	N	day	*	age, gender, negative affect	<b>DD:</b> high strain greater decline, job control predicted less decline	<b>DD:</b> demands	<b>DD:</b> (-ve) strain, control	4

Column headings: 'From time of waking'=samples anchored on waking time, yes/no; 'Shift'=study specified whether participants worked only during the day or rotating/night shifts, \*=not specified; 'Non-comp.'=measures taken to exclude non-compliant participants or samples, e.g. samples >10m outside timed protocol; 'Support for strain model and flatter DD/higher pm level?'=does this study support an association between higher job strain and a flatter diurnal cortisol rhythm, or higher evening level; 'Quality score'=rating of study methodology, described in main text

M=men; W=women; SES=socioeconomic status; CARI=cortisol increase on awakening, difference between peak and waking level; CARauc=cortisol area under the curve, based on morning samples only

**Table 4.2 Associations between psychosocial job strain and c) daily cortisol output**

First author (date)	Population, n	Work stress exposure(s)	Sampling day (s)	Procedure	Time of waking	Shift	Non-comp.	Covariates	Significant association with cortisol output	Null association with cortisol output	Support for strain and higher output?	Quality score (/10)
Maina (2009)	n=104 workers from 2 call centers (28 M, 76 W)	Strain (=quadrant term, 4 categories), demands, ERI (effort/reward as binary <=1 vs >1), overcommitment	3: 2 work, 1 leisure	7 samples: waking, +30/60m, start of work shift, +every 3 hrs <i>AUC4-7 based on samples 4-7; AUC1&amp;4-7 based on area under curve over the day</i>	Yes	day	Yes	age, gender, education level, marital status, waking time, sleep duration, sleep quality, weekdays, work schedule, adherence	<i>AUC1&amp;4-7: effort (-), reward (+) in one centre; ERI (-) in one centre</i> <i>AUC4-7: effort (-) one centre only</i>	Strain, demands, control not associated with any measures of daily output	(null)	8
Kunz-Ebrecht (2004)	n=181 UK Whitehall II cohort, (97M, 84W); high SES n=126 vs. low SES n=55	Demands, control (not strain)	1 work day	10 samples: waking, waking +30m, 8 2-hourly 30 minute intervals until 2200-2230 <i>Repeated measures ANOVA, demands &amp; control split at median</i>	Yes	*	Yes	age, waking time, smoking	W: interaction between SES and demands, highest output for low SES women with high demands M: high control associated with lower cortisol throughout the day	M: demands W: control	M: (+ve) control W: (+ve) interaction only	6
Thomas (2009)	n=7916 working adults aged 45 years, 1958 British birth cohort	Strain (=quadrant term, strain vs. other) <i>Also overtime work, regular night work</i>	1 day	2 samples only: waking +45m, waking +3h45 <i>daily output based on mean of two samples</i>	Yes	identified night workers	No	ses at birth, education, adult ses, smoking, marital status	No main effects of job strain <i>Night work associated with higher output, overtime associated with lower output in men only</i>	Strain	(null)	5
Eller (2011)	n=70 Danish working adults (22 M, 48 W)	Demands, control, support at work, ERI, effort, reward, overcommitment, weekly work hours assessed '02 and 08	1 day, assessed on 2 occasions 6 years apart	3 samples: waking, +30m, 1800 <i>Analysis by repeated measures ANCOVAs, exposures split at median</i>	Yes	*	*	age, gender, social status, time of waking, children, housework, year (2002 or 2006)	W: year only M: ERI (+), effort (+), social status (+), children (-), hours housework (-)	W: Strain, demands, control, ERI, effort, reward M: Strain, demands, control, reward	(null)	4
Fujiwara (2004)	n=16 W Japanese nurses	Strain (=demands/control, split at median for high vs. low strain)	3: 1 day shift, 1 night shift, 1 leisure	3 samples on 3 days: e.g. 0900, 1300, 1900 on leisure day. <i>Differences high vs. low strain assessed with repeated measures ANOVA</i>	No	day and night	No	age, work experience	<i>Lower cortisol over time on day shift in high strain group (F=3.9, p=0.08), neared significance</i>	Demands, control, social support at work	(null)	4
Eller (2006)	n=83 Danish working adults (28 M, 58 W)	Demands, control, support at work, ERI, effort, reward, overcommitment, time pressure (split at mean)	1 day	6 samples: waking, +20m, +30m, + 60m, +8h, 1800 <i>Repeated measures ANOVA, S1-S6</i>	Yes	*	*	age, time of first sample, physical activity, smoking	No main effects of job strain <i>Effort, ERI and overcommitment predicted higher cortisol over the day in men, ERI in women</i>	Strain, demands, control	(null)	3

Only one study, by Maina et al. (2009) assessed output via area under the curve across the day. No association with job strain was found, either including or excluding the waking sample. Four studies examined differences in the daily output using repeated measures analysis of variance with work stress exposure as a between-person variable, but none of these studies controlled for waking time, sleep, socioeconomic status and behavioural factors as potential confounders. One study used the mean of only two measures, three hours apart, to assess daily output (Thomas et al., 2009). Two studies by Eller and colleagues (Eller et al., 2006; Eller et al., 2011) described the same population of Danish adults: cross-sectional measures were repeated in 2002 and 2008. The authors did not report effects of cumulative job strain, but there was no association between strain and cortisol output at either time point.

#### *Job strain and cortisol review: summary of findings*

This review did not confirm an association between the job strain model and the cortisol awakening response, or identify a reliable association with output over the day or the diurnal decline. Variability in sampling protocols, treatment of exposure and outcome variables and adjustment for covariates meant that comparing directly between studies was not possible. The most consistent evidence was for an association between job strain and raised evening cortisol levels, with a positive association reported in four out of five studies.

Raised evening levels in association with job strain are consistent with a profile of sustained HPA axis activation and potentially inability to recover (Ursin and Eriksen, 2004). Dahlgren et al. (2005) examined diurnal cortisol rhythms within the same 34 individuals working both a highly stressful week (based on subjective ratings) and a lower stress week; greater subjective stress was associated with less sleep, longer work hours and higher evening cortisol. Major uncontrollable stressors including combat or assault have also been linked to a high, flat rhythm of cortisol in a meta-analysis by Miller et al. (2007). Studies included in the current review did not find an association between job strain and diurnal decline, but diurnal 'slope' was typically inferred from the difference in cortisol from morning to evening. Difference scores do not take into account waking or sleeping hours so a regression approach is preferable to measure the slope of decline. The peak morning sample should also be excluded, since this is under independent control of the diurnal decline (Clow

et al., 2004). In the Whitehall II cohort, high bedtime cortisol levels and a flatter diurnal slope were found to predict cardiovascular mortality (Kumari et al., 2011).

Chida and Steptoe (2009) found a significant positive association between work stress and the CAR in their meta-analysis. Only four of the same articles were included in this review, owing to different stress exposure measures. It may be that job strain is less reliably associated with the CAR than other work stress measures. Studies of within-person variation in the CAR have shown that the same individual may demonstrate both positive and negative awakening responses, with prior day negative affect and anticipation of stress both linked to a higher awakening response (Dahlgren et al., 2009; Stalder et al., 2010). It has been suggested that morning cortisol reactivity may be influenced more by immediate than by chronic strain exposure (Rystedt et al., 2008).

It has been hypothesised that a blunted diurnal profile appears only in the later stages of adaptation to chronic stress and reflects disturbed HPA axis feedback mechanisms (McEwen, 1998b). A weakness of this review was that none of the included studies examined changes in the diurnal cortisol profile over time in relation to changes in work stress.

The use of hair cortisol concentration as a retrospective indicator of systemic levels of cortisol may be an alternative method for understanding long-term changes in HPA axis activity (Staufenbiel et al., 2013). Unemployment and shift work in adults less than 40 years old have been linked to increased hair cortisol, but as yet associations with job strain or changes in strain over time have not been reported (Dettenborn et al., 2010; Manenschijn et al., 2011).

This review was limited to the inclusion of job strain as the psychosocial work exposure, but this measure has a robust association with incident heart disease (section 4.1.2). Important studies may have been omitted, but two databases and the bibliographies of relevant articles were hand-searched in order to identify relevant papers. Allocation of a quality score is controversial since the process is subjective and the score somewhat arbitrary, but given the heterogeneity of sampling protocols a one-number summary may give a useful indication of methodological quality (de Vet et al., 2003). The criteria were made



explicit and the simple ranking was designed to show whether there were any obvious patterns of association in higher versus lower scoring papers.

*Does well-being influence the association between job strain and cortisol?*

Chapter 2 (section 2.2.3) reviewed evidence which suggested a weak association between positive psychological well-being and a reduced mean cortisol output over the day, with less consistent associations reported for a lower CAR and very limited evidence linking well-being to a steeper diurnal decline. Three studies in the review in section 4.2.2 above adjusted for indicators of psychological well-being when testing the association between job strain and cortisol. In the Whitehall II cohort, Kunz-Ebrecht et al. (2004a) measured state positive affect and stress ratings over the day. Happiness was lower on work than weekend days, but subjective mood ratings were not directly correlated with the CAR, whereas demands and socioeconomic status interacted to predict a heightened CAR. The relationship between job strain and affect ratings was not described. Karlson (2011) found that both job high control and mastery both predicted a lower CAR, but did not test these variables in the same model. In the same study, higher job demands, but not mastery or psychological distress, were associated with a flatter diurnal decline. Harris et al. (2007) reported that vitality predicted a lower evening cortisol level in 40 female nursing staff, but decision authority and caffeine intake were stronger predictors of evening cortisol in a multivariable model. Sjogren et al. (2006) found that the magnitude of the diurnal decline was positively associated with life satisfaction, but in multivariable analyses only an inverse association between diurnal decline and depression remained. Job strain did not predict cortisol decline in the Sjogren study. These few studies suggest that well-being and job strain tend to predict cortisol in opposing directions, but the nature of the relationship between the two variables and cortisol has not been made explicit.

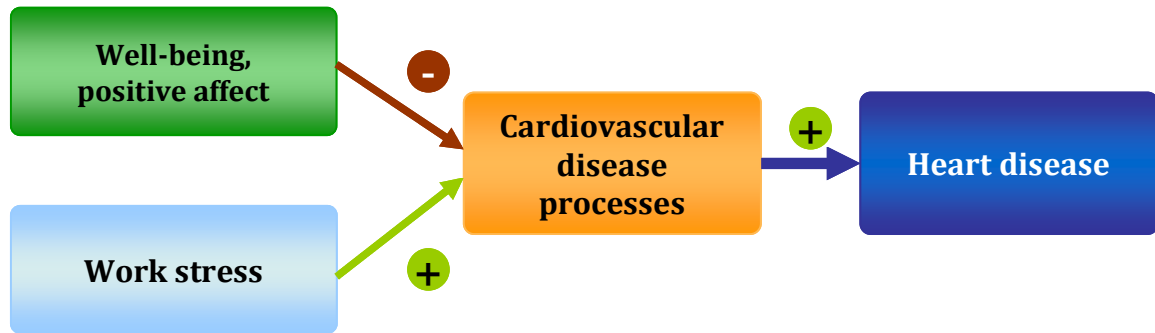
### **4.3 Potential associations between work stress, positive affect & CVD**

This chapter has summarised evidence that work stress contributes to heart disease risk. Raised ambulatory blood pressure and evening cortisol are mechanisms implicated in this association. It is not clear whether the protective effects of positive well-being on heart disease are independent of job strain. There are several plausible associations between well-

being, job strain and health outcomes. The main alternatives will be outlined below and investigated in the remaining chapters of this thesis.

*a) Do psychological well-being and strain have independent effects on heart disease?*

**Figure 4.3** Independent effects of well-being and work stress on CVD processes  
(conceptual diagram)



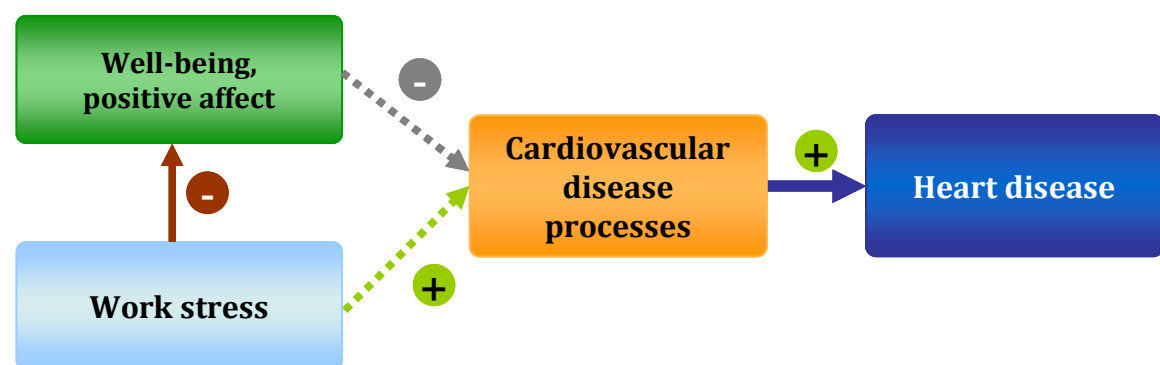
It may be that psychological well-being and work stress have opposing but independent effects on heart disease. In support of this hypothesis, a study in the Whitehall II cohort found that neither negative affect nor personality attributes such as coping style were confounders, intermediate factors, or effect modifiers of the association between job control and incident CHD (Bosma et al., 1998b), but positive affect was not examined. In a small study of 23 Swedish government workers, scores on Ryff's eudemonic well-being scales were unrelated to job demands or control (Lindfors and Lundberg, 2002). There was also no association between happiness ratings over one day and job control, job demands or job strain in 227 men and women from the Whitehall II cohort (Steptoe and Willemsen, 2004).

*b) Does low well-being mediate the association between strain and poor health?*

Poor psychological well-being may mediate the association between work stress and cardiovascular disease processes, such as raised blood pressure. A highly demanding or low control work environment could directly reduce daily opportunities to experience positive emotions and undermine psychological well-being. Job strain and effort-reward imbalance have been shown to increase the risk of common mental disorders, such as anxiety and depression (Stansfeld and Candy, 2006). Risk of major depressive disorder increased with cumulative exposure to job strain over 10 years in the Whitehall II cohort, independent of

health behaviours (Stansfeld et al., 2012). As discussed in section 1.3, depressive disorders are characterised by low positive affect, but the effects of depression and well-being on cardiovascular outcomes are thought to be at least partially independent (Boehm and Kubzansky, 2012). Harris et al. (2007) found that vitality predicted low evening cortisol, but this effect was no longer significant after adjusting for decision authority. This could be consistent with low positive affect mediating the association between job control and cortisol, but the authors did not explore this association.

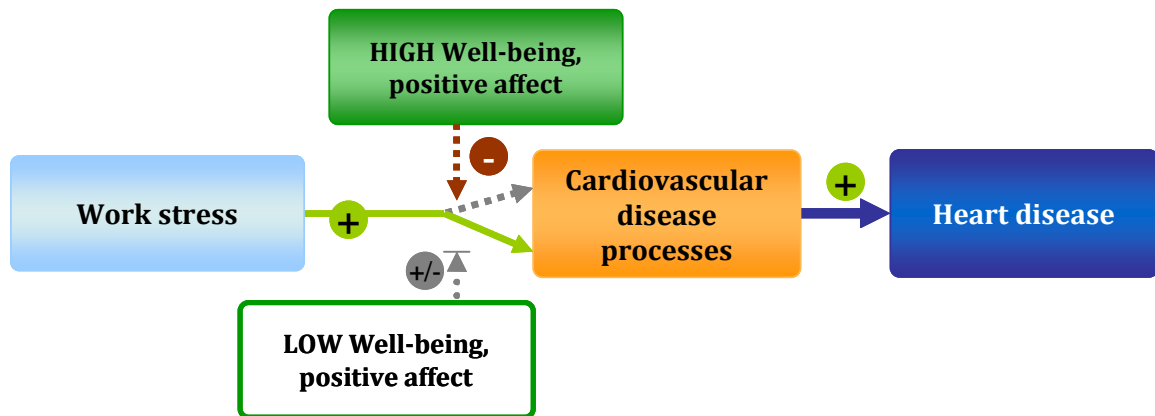
**Figure 4.4 Well-being as a partial mediator of the effects of job strain on CVD processes**



*c) Does well-being moderate the association between strain and poor health?*

It is plausible that psychological well-being might interact with job strain to moderate the association with health outcomes. This might help to explain why direct effects between job strain and physiological outcomes such as cortisol have been inconsistent. Several studies have suggested that the relationship between job strain and cardiovascular outcomes is dependent on other vulnerabilities, such as adverse socioeconomic conditions, or gender (von Bonsdorff et al., 2012; Westerlund et al., 2012). Social support has been shown to buffer the effects of work stress on cardiovascular outcomes (Johnson et al., 1989). Supportive social relationships are one factor contributing to psychological well-being (Zhou et al., 2010), but to my knowledge the potential of well-being as a moderator of the physiological effects of job strain has not been reported.

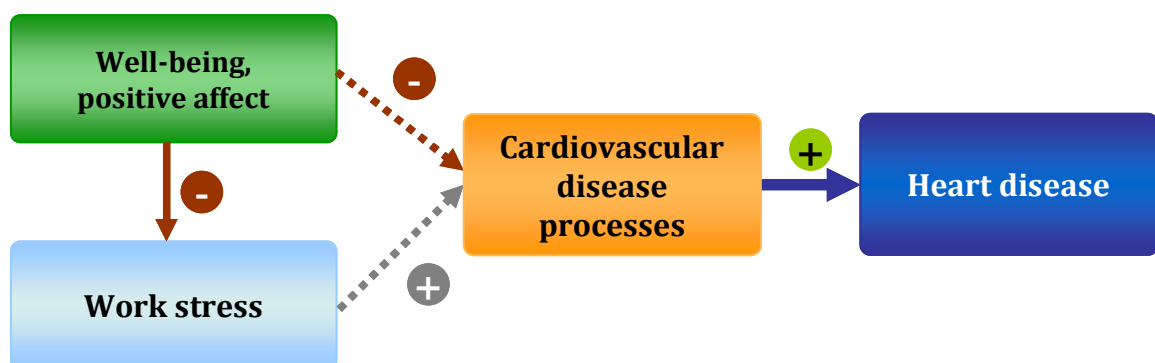
**Figure 4.5 High positive affect buffering effects of job strain on CVD processes**  
Low well-being has no influence on the association



*d) Does psychological well-being reduce perceptions of job strain?*

The final scenario which I will investigate in this thesis is whether psychological well-being is a protective or resilience factor against psychosocial job strain. Chapter 3 showed that positive emotional style was associated with greater perceptions of task control and less subjective stress in response to an acutely stressful task. If positive well-being is similarly associated with lower perceptions of job strain in the context of chronic exposure to a stressful work environment, this could partly explain the protective effects of well-being on cardiovascular outcomes.

**Figure 4.6 Psychological well-being influencing perceptions of work stress**  
resulting in a reduced influence of job strain on CVD processes



To my knowledge, this pathway has not been investigated in prospective studies with objective health outcomes. There is some support from the organisational psychology

literature that dispositional affective characteristics influence appraisal of occupational stress and job satisfaction (Elliott et al., 1994; Bowling et al., 2008), but this research has drawn conclusions mostly from cross-sectional studies, which cannot confirm temporal associations. For example, Fogarty et al. (1999) found that positive and negative affectivity independently influenced the association between occupational stressors and psychological strain. The authors suggested that employees high in positive affectivity, based on PANAS, either did not encounter as many stressors as others or did not notice them. However, these conclusions were not supported by any objective assessment of work stressors or strain.

I identified only one study which examined the longitudinal association between job strain, using the demand-control model, and an indicator of psychological well-being. Armon et al. (2012) measured demands, control, social support and vigour in 909 adults employed in the same job role on three occasions over four years. Baseline vigour, characterised as heightened physical, emotional and cognitive energy, predicted increased job control and social support over later time points, after adjusting for neuroticism. Gains in job control also predicted gains in well-being at later time points, suggesting a reciprocal relationship between these variables.

Armon et al. (2012) did not measure objective health outcomes, objective work characteristics or eudemonic aspects of well-being. The authors did not attempt to manipulate well-being or work environment characteristics. It is unclear why some employees experienced improved vigour and whether subsequent changes in self-reported control were owing to perceptual changes or active behaviours to promote a change in work conditions. If psychological well-being could be improved deliberately to subsequently improve perceptions of job control or reduce demands, this could potentially have important public health consequences for the alleviation of health risks associated with job strain.

#### *Outline for remaining chapters in this thesis*

The remaining chapters in this thesis investigate the hypotheses illustrated in Figures 4.2 to 4.6 above. Chapter 5 explores the associations between psychosocial and objective work exposures and psychological well-being in two large cross-sectional surveys of employees. These analyses test the plausibility of associations between job strain with well-being and

self-reported health outcomes, including whether well-being may be independent (Figure 4.2), a mediator (Figure 4.3) or moderator (Figure 4.4) of strain-health associations.

Chapter 6 investigates the associations between job strain, positive affect and the diurnal cortisol rhythm, whilst attempting to address some of the limitations identified in the review of job strain and cortisol studies in section 4.2.2 above. The association between job strain and cortisol is examined under different shift conditions, taking into account affect ratings over the day, to test the mediation model (Figure 4.3).

Chapters 7 and 8 concern the model outlined in Figure 4.6. Chapter 7 reviews the evidence relating to interventions which have attempted to directly improve workers' psychological well-being. Chapter 8 describes a randomised controlled trial which aimed to increase worker well-being and reduce perceptions of job strain, without altering the work environment.

## **Chapter 5 Cross-sectional associations between job strain, positive affect and fatigue in airline pilots**

In this chapter, I describe the analysis of two cross-sectional surveys conducted in an employee sample of commercial airline pilots. The study design and hypotheses are introduced in section 5.1. In section 5.2, I explain the survey methodology and the statistical approach. Sections 5.3 and 5.4 discuss the results and implications. This study demonstrates that job strain has independent associations with positive and negative affect. The findings also suggest that positive and negative affect may mediate the association between job strain and health outcomes.

### **5.1 Introduction**

The aim of this study was to explore the association between the psychosocial work environment, positive psychological well-being and self-reported physical health outcomes. Understanding these relationships may be important for prevention: if positive well-being is involved in the pathways linking job strain and health, interventions to increase general well-being might protect against the adverse consequences of job strain.

#### *Study design*

The focus of this thesis is heart disease so the preferred study design to investigate the association between job strain, well-being and health outcomes would be a prospective study in which a cohort of disease-free workers are followed up for incident heart disease over time. Repeated assessments of work exposures and well-being would allow the temporal relationship between the variables to be investigated. To my knowledge, only one study has used a prospective design to examine affect as a potential mediator of strain-CHD associations. Bosma et al (1998) reported that negative affectivity was not a mediator or moderator of the association between job control and CHD in the Whitehall II study over 5 years. The authors did not examine positive affect states or traits.

The development of atherosclerosis occurs gradually over decades and it could be that measuring incident disease outcomes may not be sensitive to small mediation or moderation

effects associated with exposures and affective experience years earlier. One less resource-intensive alternative to conducting a longitudinal cohort study is to examine the association between concurrent work exposures and 'intermediate' physical health outcomes associated with heart disease in an at-risk population. I analysed data from cross-sectional employee surveys of airline pilots in 2010 and 2012 to investigate the relationships between job strain and positive affect with two self-reported health outcomes: sleep quality and fatigue. Prospective studies have reported that both poor sleep quality and fatigue are associated with an increased risk of heart disease in healthy middle-aged population cohorts (Hoevenaars-Blom et al., 2011; Ekman et al., 2012). The 2010 employee survey was completed anonymously so responses could not be linked to 2012. The surveys were analysed separately to show the consistency of associations.

### *Study population*

This study was conducted in airline pilots employed by one low-cost airline. This sample provided several advantages for the analysis of psychosocial work exposures and health outcomes compared with other single occupation samples. Firstly, all participants were pilots employed by the same short-haul airline which employed a rotating shift system. Participants therefore experienced similar physical day-to-day working conditions and contractual obligations. Pilots' duty and flight hours are regulated by the Civil Aviation Authority (CAA) and working hours are logged electronically. The influence of psychosocial measures of work stress on health outcomes could therefore be compared with recent objective records of work history (physical demands). Secondly, pilots with serious chronic health conditions including heart disease and cancer are not permitted to fly. All employees had annual medical screenings to confirm their fitness. Chronic illness was therefore unlikely to influence any association between job strain and self-reported health outcomes. Thirdly, this population had limited variability in occupational status and financial rewards; pilots were ranked either as First Officers or Captains, with a salary corresponding to years of experience, enabling these potential confounders to be controlled for in the association between job strain and health outcomes.

### *Health outcomes: fatigue and sleep problems*

Employee surveys in 2010 and 2012 were part-funded by BALPA, the British Association of Airline Pilots, to investigate pilot fatigue. Pilot fatigue is a risk factor for aircraft accidents and



therefore prevention of fatigue is shared responsibility between pilots and their employers (Goode, 2003). Fatigue can be defined as extreme tiredness associated with a lack of energy, mental exhaustion, poor muscle endurance, delayed recovery after physical exertion, and non-restorative sleep (Rosenthal et al., 2008). Fatigue is a common symptom in chronic illness (Whitehead, 2009). In healthy pilots, irregular sleep and work shifts, long duty hours and flying multiple sectors<sup>12</sup> have been linked to increased fatigue (Petrie et al., 2004; Powell et al., 2007; Spencer and Robertson, 2007; Powell et al., 2008).

Studies in general population samples have identified psychosocial work stress as a contributor to fatigue. For example, de Lange et al. (2009) followed over 1,700 employees in the same job role over three years. Cumulative exposure to a high strain work environment predicted higher fatigue and poorer sleep quality. There was no support for a reverse association; sleep quality and fatigue did not predict increased job strain over time. Similarly, in a longitudinal study of 5,000 Swedish workers, psychological job demands, low job control and low job support predicted exhaustion one year later, even after adjusting for physical workload and potential confounders such as disease and lifestyle factors (Lindeberg et al., 2010). No studies to date have reported the association between psychosocial job strain and sleep or fatigue within pilots.

Sleep is an important restorative process which is essential for physiological balance and long-term health and mental functioning (Åkerstedt et al., 2009). Both poor sleep quality and insufficient quantity are associated with fatigue (Oginska and Pokorski, 2006; Rosenthal et al., 2008). For example, a recent longitudinal study in adolescents demonstrated that poor sleep quality predicted fatigue six and 12 months later (Tham et al., 2013). Fatigue and sleep problems may also occur independently of one another (Rosenthal et al., 2008). For example, in a large Swedish population survey with over 58,000 participants, 33% reported fatigue and 13% reported sleep disturbances. Female gender, illness, hectic work, physically strenuous work and shift work were associated with both sleep difficulties and fatigue in cross-sectional analyses. Younger age (<50 years) was associated with fatigue whereas older age predicted sleep problems. Overtime work predicted fatigue, but not sleep difficulties (Åkerstedt et al.,

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<sup>12</sup> One sector is the equivalent of one take-off and one landing. A single commercial flight might include multiple sectors if it includes a stop to re-fuel or pick up additional passengers.

2002). This study shows that although sleep problems and fatigue are closely related, they may have some unique predictors.

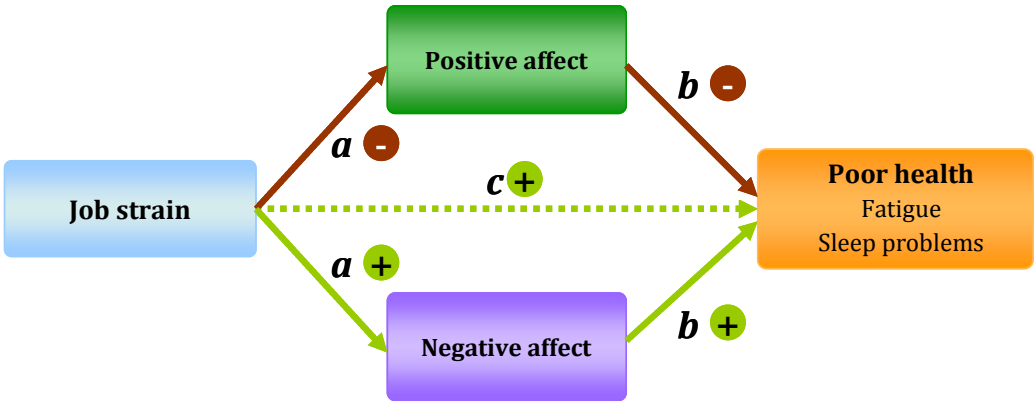
### *Measures of well-being*

As discussed in Chapter 4, job strain is an established risk factor for negative mood disorders (Stansfeld and Candy, 2006). I hypothesised that high job strain would be associated with both high negative affect and low positive affect, and that these associations would be independent of one another. Affect in the current study was based on the frequency of positive and negative moods using items from the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983; Denollet et al., 2008). Four positive items included feeling cheerful, being able to enjoy things, seeing the funny side of things and looking forward with enjoyment to things over the last two weeks. Positive affect in this study can therefore be considered a retrospective measure of hedonic well-being, which included an aspect of hopefulness or optimism. Negative affect items included feelings of dread, panic, tension and worry; items which were taken from both anxiety and depression subscales.

Symptoms of anxiety and depression have been shown to predict sleep problems, though reciprocal associations have been reported (Gillespie et al., 2012; Rosenstrom et al., 2012). One cross-sectional study in older adults reported that both hedonic and eudemonic well-being were positively associated with self-reported sleep quality, independent of chronic life stressors including financial strain, poor social relationships and psychological distress (Steptoe et al., 2008b). A three year study in working adults found evidence for reciprocal inverse relationships between self-reported insomnia and well-being assessed with the Shirom-Melamed Vigour measure, which assesses both vitality and emotional engagement at work (Armon et al., 2013).

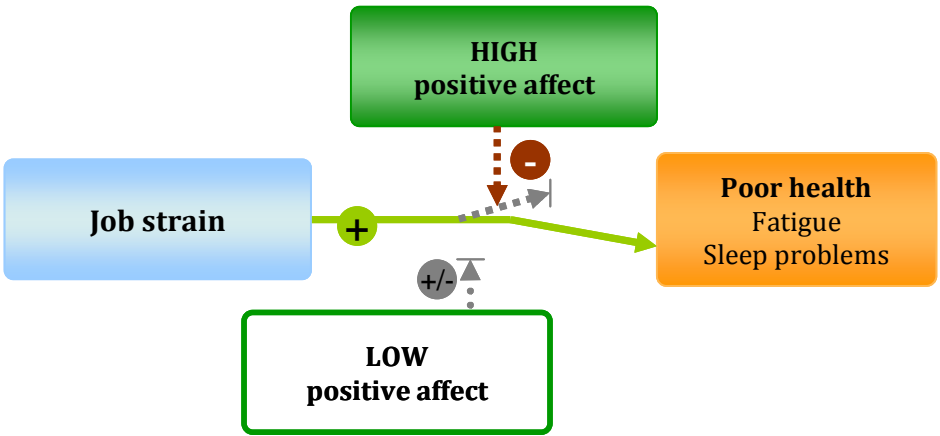
I hypothesised that both positive and negative affect may mediate the association between job strain and poor health outcomes (Figure 5.1). To explore indirect pathways, a series of hierarchical regression analyses were conducted using PROCESS, a conditional process modelling approach (Hayes, 2012). All variables were assessed at the same time in this cross-sectional study, so modelling could only be used as a preliminary test of the plausibility of the hypothesised associations; temporal relationships could not be confirmed.

**Figure 5.1** Positive and negative affect mediating the association between psychosocial job strain and health outcomes via indirect a and b pathways  
 A direct pathway, c, may also link job strain and health outcomes



As an alternative to the mediation pathway illustrated in Figure 5.1, I explored whether positive affect could moderate the association between job strain and poor health. As outlined in section 4.2.3, high positive affect may buffer the association between job strain and health outcomes, such that pilots with high positive affect would have low fatigue scores, regardless of job strain (Figure 5.2). I expected that either the mediation or moderation would be the dominant pathway. It has been argued that the same variable cannot both mediate and moderate the association between a predictor and an outcome simultaneously in a simple three variable model (Jacoby and Sassenberg, 2010).

**Figure 5.2** Positive affect as a moderator: high positive affect buffering the association between job strain and health outcomes



### 5.1.1 Hypotheses

Based on the pathways introduced in section 4.3 and illustrated in the introduction above, I hypothesised that either:

- Hypothesis 1: There will be an inverse association between job strain and positive affect, which will be statistically independent of negative affect;
- Hypothesis 2: Positive and negative affect will mediate the association between job strain and fatigue, and between job strain and sleep problems

OR

- Hypothesis 3: High positive affect will buffer the association between job strain and health outcomes; job strain will have a weaker association with health outcomes in individuals high in positive affect.

## 5.2 Methods

### *Participants*

All BALPA members employed by one low-cost airline across the UK, Germany, France and Italy were eligible to participate (n=1,190). BALPA membership included approximately 80% of the pilots employed by the company. Pilots worked a 5-3-5-4 shift pattern consisting of 5 early shifts (pre 6am start), 3 rest days, 5 late shifts (post 12 noon start) and 4 rest days. In 2010, 493 pilots returned a questionnaire, an estimated response rate of 41.4%. Returned postal surveys missing data for age, rank and sex were excluded (n=9). Participants missing more than 20% of items for job strain, affect or fatigue were excluded (n=30). If up to 20% of the items within a single scale were missing, a score was computed based on the mean value of remaining items. In 2012, 212 pilots returned a complete online questionnaire, a 17.8% response rate. In order to standardise objective work exposures within each sample, part-time workers (7.7-8.1%) were excluded from this analysis (2012 n=36, 2010 n=17) leaving a study sample of n=418 in 2010 and n=195 in 2012.

### *Procedures*

BALPA informed their members via a routine membership email that researchers from UCL were conducting a survey to investigate factors associated with fatigue. In 2010, BALPA posted the study questionnaire to members individually. A return postage paid envelope to

UCL was provided. In 2012, at the request of BALPA, I converted the questionnaire to an online survey using Opinio™ software. BALPA emailed their members a hyperlink to access the survey. In both years, questionnaires were distributed in mid-October and responses were accepted until mid-December. Responses were provided anonymously. Members were sent fortnightly email reminders from BALPA to complete the surveys, but there was no direct contact from UCL to BALPA membership.

### *Measures*

The questionnaire included sections on demographic characteristics, recent flight history, psychosocial work environment, health behaviours, fatigue, sleep problems and mental well-being. The content of the 2012 questionnaire was identical to 2010 but the survey was completed online. All questionnaires were completed in English which is the language used in all European flight operations. A copy of the questionnaire is included in the Appendix for Chapter 5.

*i) Demographic characteristics:* age (20-29 / 30-39 / 40-49 / 50-59 years), gender, years of experience working as a pilot, rank (first officer / captain), country (UK / France / Germany / Italy).

*ii) Objective work history:* participants were asked to extract data from their electronic flight logs for the number of hours flown over the preceding 6 months (<350 / 350-424 / 425-500, >500 hours), duty hours, flying hours and sectors flown over the last 28 days. Previous pilot fatigue research has stressed the importance of combining multiple objective work measures to predict fatigue (Spencer and Robertson, 2007). A summary objective work index was derived by dividing each objective work measure at the median; scores above the median were assigned a value of 1 and below the median a value of 0. All four items were summed to give a work index score ranging from 0-4, with higher scores indicating a more intensive work history.

*iii) Psychosocial work factors:* psychosocial work stress was evaluated according to Karasek and Theorell's job strain model (Karasek, 1979; Karasek and Theorell, 1990). Job strain was computed from separate scales of work demands (4-items) and job control (15-items) taken from the Whitehall II Job Characteristics Questionnaire (Bosma et al., 1997). All questions were answered on a 4-point scale, scored from 1 to 4, from 'often' to 'never, or almost never' with higher scores indicating higher demands and higher control. A continuous job strain

scale was derived using the quotient approach, job strain = demands / control (Steptoe et al., 2000a), where demands and control were based on the mean score per item (possible range 1-4). To compare demands and control scores with the Whitehall II cohort of civil servants, scores for both scales were summed (range: demands 5-16 out of 16, control 19-51 out of 60) and converted to percentage scores from 0 to 100 (demands % = (sum-4)/12\*100, control % = (sum-4)/56\*100) (Steptoe and Willemsen, 2004). Social support from colleagues and immediate superiors was also measured using 6-items from the Whitehall II questionnaire. Scores were summed and re-scaled from 0 to 100 similarly to demands and control, with higher scores indicating greater social support. Cronbach's alpha ( $\alpha$ ), a measure of internal validity, was 0.57 for demands, 0.79 for control and 0.77 for social support in 2010.

*iv) Health behaviours:* diet, smoking, exercise and alcohol consumption were measured as potential confounders in the association between job strain and health outcomes (Chandola et al., 2008). Diet was measured as the number of items of fruit and vegetables portions consumed on a typical work day. Smoking was categorised as current or non-smoker. Exercise was measured as the typical number of times per week practicing 30 minutes or more physical exercise. The RAPS4 alcohol screening questionnaire, a brief 4-item screening instrument, was used to identify potential alcohol misuse (Cherpitel, 2000). Participants were asked if they had felt guilt after their drinking, could not remember things they said or did after drinking, failed to do what was normally expected after drinking, or had a morning drink in the last six months. Alcohol misuse (positive / none) was indicated by one or more positive responses.

*v) Fatigue:* measured with the Fatigue Severity Scale (FSS), which has been validated in both clinical and healthy populations and shows good test-retest reliability (Krupp et al., 1989; Lerdal et al., 2005). Respondents rated 9-items relating to the impact of fatigue on functioning and behaviour over the last two weeks on a scale from '1' indicating no fatigue to '7' indicating severe fatigue. Mean FSS was used as a continuous measure of fatigue (Cronbach  $\alpha$  = 0.85). A cut-off of  $\geq 5.0$  was used to assess the prevalence of clinically significant fatigue, an estimated two standard deviations above the level of healthy controls (Lerdal et al., 2005).

*vi) Sleep problems:* assessed with the Jenkins Sleep Problems Scale. The scale contains 5-items assessing the frequency respondents experience trouble falling asleep, waking up in the night, difficulty staying asleep, waking up feeling tired and disturbed or disturbed sleep (Jenkins

1988). Responses were given along a 6-point scale from '1' not at all to '6' 21 to 31 nights per month. Scores were re-scaled from 0 to 100 (as per demands and control), with higher scores indicating greater sleep problems (Cronbach  $\alpha$  =0.85). This measure has previously been found to be inversely related to psychological well-being (Steptoe et al., 2008b).

vii) *Positive affect*: the frequency of experiencing positive affect over the last two weeks was assessed using four positive items (feels cheerful/ looks forward with enjoyment to things/ still able to enjoy things/ sees the funny side of things') from the 14-item Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983). In an exploratory factor analysis, these items loaded onto one dimension, which was distinct from a negative affective dimension (Denollet et al., 2008). Negative affect was also measured with four items (fears something awful will happen, feelings of panic, frequently worries, feels tense). Items were rated on a 4-point frequency scale and summed so that higher scores indicated higher levels of affect. Cronbach's alpha was 0.82 for positive affect and 0.80 for negative affect, indicating high internal consistency. Positive affect based on this measure has previously been linked to reduced mortality in coronary stent patients (Denollet et al., 2008).

### *Statistical analysis*

Questionnaires were completed anonymously so individual responses could not be linked over time. Only 40% of 2012 respondents recalled completing a survey in 2010. Responses in 2010 and 2012 were therefore analysed separately so that the consistency of associations could be observed. Analyses were conducted with IBM SPSS Statistics version 21.

Years of experience as a pilot was grouped into quartiles since data had an uneven positive skew. All other continuous variables approximated a normal distribution. Health behaviours were grouped into binary variables, with the healthier option as the index category. Diet was grouped into ( $\geq 2$  /  $< 2$ ) portions of fruit/vegetables per day. Physical activity was categorised as the days per week of 30 minutes exercise ( $\geq 2$  days/ $< 2$  days). Independent t-tests for continuous data and Chi-squared tests for categorical variables were used to highlight significant differences in participant characteristics between 2010 and 2012.

Relationships between work exposures, affect and health outcomes were first tested with Pearson's product-moment correlation coefficients. The relationship between job strain

and positive affect was tested in hierarchical linear regression models on positive affect scores. The model was adjusted for demographic (age, sex, rank and years of experience), behavioural (diet, smoking, exercise, alcohol misuse) and objective work correlates, plus negative affect. Standardised z-scores with a mean of 0 and a standard deviation of 1 were computed for all continuous variables used in linear regression analyses, to aid comparisons between models with different outcomes. Un-standardized regression coefficients (B) and 95% confidence intervals (C.I.) are listed in the text.

Associations between job strain and i) fatigue ii) sleep problems were tested in separate hierarchical linear regression models. In the first step, job strain was entered to confirm the hypothesised main effect. Positive affect and negative affect were then entered; a likely mediation effect was indicated by a significant main effect of affect and a reduction in the regression coefficient for job strain (Rose et al., 2004). Moderation effects were then tested by entering product terms representing the two-way interaction (job strain x positive affect, job strain x negative affect) into the same model as covariates. Significant two-way interactions indicated a moderation effect. Regression slopes for job strain and outcomes were plotted for high vs. low positive affect individuals (split at the median) to visualise moderation effects.

To confirm indirect effects identified via linear regression, I used PROCESS, a conditional process modelling program that utilizes an ordinary least squares or logistic-based path analytical framework to test for both direct and indirect effects (Hayes, 2013). For mediation, PROCESS model 4 was used which allows multiple mediators and covariates. PROCESS allows mediation to occur when there is a relation between a predictor (i.e. job strain) and a mediator (i.e. positive affect, negative affect) and between a mediator and outcome (i.e. fatigue or sleep problems). PROCESS model 1 can be used to test the effects of a single moderator (positive affect) and multiple covariates (including negative affect). A direct relation between predictor and outcome may or may not be present (Hayes, 2009). Separate models were conducted for fatigue and sleep problem outcomes in 2010 and 2012. Work history, demographic characteristics and health behaviours were included as covariates for each association in the model. All indirect effects were subjected to follow-up bootstrap analyses with 1,000 bootstrap samples and a 95% confidence interval.



### 5.3 Results

#### *Descriptive statistics*

Participant characteristics are listed in Table 5.1. Most survey respondents were aged 30-49 years, over 70% were based in the UK and the vast majority were male; characteristics which were broadly representative of the wider employee base. Respondents from outside the UK were based in Germany (n=47, 11.2%), France (n=41, 9.8%) and Italy (n=33, 7.9%) in 2010, which corresponded closely to the distribution of BALPA members. In 2012, only 1 respondent came from Germany, 9.2% from France and 10.3% from Italy. BALPA suggested that the difference in survey response rates was due to problems contacting members by email in Germany in 2012.

Few pilots met Department of Health recommendations for exercise and diet; 46% consumed fewer than two portions of fruit or vegetables per day (versus the recommended five portions per day) and approximately half exercised for 30 minutes less than twice per week (recommended five times per week) (NHS, 2011). One in five pilots scored positive on the RAPS-4 screening questionnaire for alcohol misuse in 2010 and 1 in 4 respondents in 2012. (Normative comparison data for the RAPS4 is not available).

In 2012, pilots were more likely to report having accumulated 425 or more hours over the previous six months than in 2010, but recorded fewer duty hours and sectors over the most recent 28 days. The Civil Aviation Authority imposes an absolute maximum of 900 flying hours over 12 months (CAA, 2004). Overall the summary work index, derived from the number of objective measures a participant worked above the median (range 0-4), was not significantly different in 2010 and 2012. Work index scores were evenly distributed, for example, in 2010 scores were '0' 16.3%, '1' 23.0%, '2' 23.0%, '3' 17.0%, '4' 20.8%.

**Table 5.1 Characteristics of survey respondents in 2010 and 2012**

	2010, % n=418	2012, % n=195
Age 20-39 years	51.4	52.3
Age 40-64 years	48.6	47.7
Male	96.2	95.7
Captain	62.7	62.0
Based in the UK	71.1	79.9**
Years as a pilot, mean (SD)	13.6 (8.9)	12.8 (8.1)
<i>Health behaviours</i>		
<2 portions fruit/veg per day	46.9	41.8
Current smoker	7.7	8.3
Exercise <2 times per week	50	46.5
Alcohol misuse, RAPS-4 +ve	20.3	27.2
<i>Objective work history</i>		
>425h flying last 6 months	53.5	66.7*
Sectors, last 28d, mean (SD)	31.8 (10.6)*	29.4 (11.4)
Flying hours, last 28d, mean (SD)	60.5 (20.9)	57.8 (19.6)
Duty hours, last 28d, mean (SD)	124.6 (31.8)**	111.2 (31.9)
Summary work index 0-4, mean (SD)	2.03 (1.37)	2.06 (1.25)
<i>Psychosocial strain</i>		
Demands, mean % (SD)	70.1 (12.6)	70.3 (12.6)
Control, mean % (SD)	54.9 (9.0)	58.8 (8.3)**
Job strain, mean (SD)	1.32 (0.37)*	1.23 (0.31)
Social support, mean % (SD)	62.8 (17.5)	62.9 (18.1)
<i>Affective measures</i>		
Positive affect, mean (SD)	8.3 (2.4)	8.1 (2.5)
Negative affect, mean (SD)	3.7 (2.5)	4.6 (2.6)**
<i>Physical health</i>		
Fatigue, mean (SD)	4.7 (1.0)	4.8 (1.0)
Sleep problems, mean (SD)	53.7 (18.1)	56.4 (18.5)

\*<0.05, \*\*<0.001 Chi-squared test for categorical variables, independent t-test for continuous variables

Job strain scores ranged from 0.44 to 3.16 in 2010, and from 0.59 to 2.00 in 2012. Higher levels of job control and lower levels of job strain were reported by respondents in 2012. For reference, levels of job control, demands and social support can be compared to a sample of over 2,100 male civil servants in the Whitehall II study, from across all grades of the civil service, recruited for a substudy of heat shock proteins in 2003-4 (Marmot and Brunner, 2005; Steptoe et al., 2007c). In both survey years, pilots' responses were associated with higher levels of psychosocial work strain than the civil servant population: higher demands

(2010 survey  $70.1 \pm 12.6$ ; Whitehall  $58.8 \pm 20.4$ ), lower job control (2010 survey  $54.9 \pm 9.0$ ; Whitehall  $70.2 \pm 18.0$ ) and lower social support (2010 survey  $62.8 \pm 17.5$ ; Whitehall  $75.5 \pm 19.5$ ).

Positive and negative affect scores across the full range from 0 to 12 were reported in both 2010 and 2012. Significantly higher levels of negative affect were reported by 2012 respondents. Pilots reported lower levels of both positive affect (2010 survey  $8.4 \pm 2.4$ ; patients  $9.4 \pm 2.9$ ) and negative affect (2010 survey  $3.7 \pm 2.5$ ; patients  $6.5 \pm 2.1$ ) than a French patient sample of 874 coronary stent patients (Denollet et al., 2008)..

Fatigue Severity Scale (FSS) scores ranged from 1.1-7.0. Pilots' mean scores were significantly higher than fatigue scores for healthy adults in the original FSS validation study (2010 survey  $4.7 \pm 1.0$ ; Krupp et al. (1989)  $2.3 \pm 0.7$ ) or a Swiss population survey of 454 adults ( $3.0 \pm 1.8$ ) (Valko et al., 2008). Sleep problems were much more prevalent in the pilot surveys than in 486 older men from the Whitehall II study, mean age 61 years (2010 survey  $53.7 \pm 18.1$ ; Whitehall  $25.4 \pm 21.9$ ) (Steptoe et al., 2008b).

#### *Correlations between psychological, sociodemographic and behavioural characteristics*

In 2010, job strain was weakly positively correlated with older age ( $r = 0.15$ ,  $p = 0.002$ ) and years working as a pilot ( $r = 0.18$ ,  $p < 0.001$ ) but was not associated with gender or rank. These correlations were not significant with the smaller sample in 2012. Positive affect had a weak negative correlation with years as a pilot in 2010 ( $r = -0.11$ ,  $p = 0.030$ ) and with higher rank ( $r < -0.12$ ,  $p < 0.05$ ) meaning that more experienced pilots, who were more likely to be ranked Captain, tended to report lower positive affect. Age, gender, rank and years experience were not directly correlated with fatigue, sleep problems or objective work index.

Job strain was correlated with consuming fewer fruit and vegetables in 2010 and 2012 ( $r > 0.20$ ,  $p < 0.003$ ) and with smoking in 2012 ( $r = 0.24$ ,  $p = 0.001$ ). Positive affect had opposite correlations of similar magnitude with poor diet and smoking in both years. Objective work index was not correlated with health behaviours. Fatigue and sleep problems were weakly associated with alcohol misuse ( $r > 0.10$ ) and physical inactivity ( $r > 0.119$ ,  $p < 0.05$ ) in both years, but were not directly associated with diet or smoking.

*Patterns of association between work characteristics, affect and health outcomes*

Table 5.2 lists correlations between work exposures, affect, fatigue and sleep problems in 2010 and 2012, to illustrate the patterns of associations and consistency across years. Job strain had a moderate inverse association with positive affect ( $r < -0.41$ , both years) and a positive association with negative affect ( $r > 0.40$ , both years). Higher job strain, and the components of higher demands and lower control, were positively correlated with fatigue and sleep problems. Social support had a weak inverse association with fatigue in 2010 only ( $r = -0.17$ ,  $p < 0.05$ ) and with sleep problems in 2010 and 2012 ( $r < -0.14$ ,  $p < 0.05$ ). Fatigue and sleep problems were positively correlated in both years ( $r > 0.41$ ,  $p < 0.001$ ).

Psychosocial job strain was only weakly correlated with the objective work summary index (2010  $r = 0.12$ ; 2012  $r = 0.16$ ,  $p < 0.05$ ). Objective work history was weakly associated with positive and negative affect in 2010, but correlations in 2012 were not significant. Objective work index weakly predicted higher sleep problems in 2010 ( $r = 0.11$ ,  $p < 0.05$ ) and fatigue in 2012 ( $r = 0.17$ ,  $p < 0.05$ ). Fatigue was positively associated with the individual measures making up the work index, but associations were weaker and less consistent than with the overall index. For example, in 2010, fatigue was weakly correlated with hours flown in the last 6 months ( $r = 0.11$ ,  $p = 0.036$ ) but only weakly associated with hours flown in the last 28 days ( $r = 0.09$ ,  $p = 0.071$ ) and not significantly linked to sectors ( $r = 0.02$ ,  $p = 0.729$ ) or duty hours ( $r = < 0.01$ ,  $p = 0.973$ ). In 2012, fatigue was correlated with sectors flown ( $r = 0.14$ ,  $p = 0.044$ ) and hours flown in the last 28 days ( $r = 0.18$ ,  $p = 0.009$ ) but not with duty hours or hours flown in the last 6 months ( $r = > 0.10$ ,  $p > 0.300$ ).

**Table 5.2 Pearson product moment correlation coefficients**  
2010 correlations are shown in the left of the table; 2012 correlations are upper right (shaded)

Variables	1	2	3	4	5	6	7	8	9
1. Job demands		-.173*	-.059	<b>.810**</b>	.088	<b>-.329**</b>	<b>.347**</b>	<b>.273**</b>	.222*
2. Job control	<b>-.212**</b>		<b>.400**</b>	<b>-.697**</b>	<b>-.187**</b>	<b>.328**</b>	-.232*	-.225*	<b>-.259**</b>
3. Social support	<b>-.189**</b>	<b>.345**</b>		<b>-.266**</b>	-.121	<b>.315**</b>	<b>-.249**</b>	-.064	-.150*
4. Job strain	<b>.786**</b>	<b>-.733**</b>	<b>-.348**</b>		.161*	<b>-.448**</b>	<b>.401**</b>	<b>.331**</b>	<b>.317**</b>
5. Work index <sup>a</sup>	.128*	-.060	-.043	.118*		-.062	.089	.165*	-.016
6. Positive affect	<b>-.349**</b>	<b>.338**</b>	<b>.234**</b>	<b>-.440**</b>	-.121*		<b>-.634**</b>	<b>-.395**</b>	<b>-.321**</b>
7. Negative affect	<b>.384**</b>	<b>-.240**</b>	<b>-.218**</b>	<b>.400**</b>	.124*	<b>-.532**</b>		<b>.455**</b>	<b>.362**</b>
8. Fatigue	<b>.343**</b>	<b>-.246**</b>	-.166*	<b>.369**</b>	.079	<b>-.482**</b>	<b>.442**</b>		<b>.413**</b>
9. Sleep problems	<b>.313**</b>	<b>-.203**</b>	-.136*	<b>.314**</b>	.107*	<b>-.435**</b>	<b>.439**</b>	<b>.531**</b>	

\*<0.05, bold\*\*<0.001. a=summary objective work index (flying hours last 6 months, flying hours, duty hours and sectors last 28 days)

### 5.3.1 Hypothesis 1: Job strain will be inversely associated with positive affect

In 2010, in an unadjusted regression model, job strain was negatively associated with positive affect ( $B = -0.440$ , 95% C.I.  $-0.527$  to  $-0.354$ ,  $p < 0.001$ ), and explained 19.4% of the variance, based on  $R^2$ . When objective work history, age, sex, years as a pilot, smoking, poor diet, physical inactivity and alcohol misuse were added to the regression model, only job strain ( $B = -0.403$ , C.I.  $-0.493$  to  $-0.313$ ,  $p < 0.001$ ) and smoking ( $B = -0.376$ , C.I.  $-0.700$  to  $-0.052$ ,  $p = 0.023$ ) were associated with positive affect. The regression coefficient for job strain decreased by a further 40% when negative affect was added to the model, but job strain remained a significant predictor of positive affect (Table 5.3).

Data for 2012 demonstrated a similar pattern. In an unadjusted model, job strain explained 20.1% of the variance in positive affect ( $B = -0.448$ , C.I.  $-0.512$  to  $-0.240$ ,  $p < 0.001$ ). Adjustment for covariates reduced the regression coefficient for job strain by 20% ( $B = -0.376$ , C.I.  $-0.512$  to  $-0.240$ ,  $p < 0.001$ ). Infrequent fruit and vegetable consumption was also inversely associated with positive affect. When negative affect was added to the model, the regression coefficient for the association between job strain and positive affect reduced by a further 42% but remained significant ( $B = -0.219$ , C.I.  $-0.339$  to  $-0.100$ ). Significant predictors of positive affect in the final regression models for 2010 and 2012 are listed in Table 5.3 below.

**Table 5.3 Multiple regression analyses to predict positive affect in 2010 and 2012**

2010				2012			
Predictor	$\beta$	B	95% C.I.	Predictor	$\beta$	B	95% C.I.
Job strain	-.242	-.242**	-.330 to -.154	Job strain	-.219	-.219**	-.339 to -.100
Smoking	-.090	-.337*	-.631 to -.044	Poor diet	-.128	-.258*	-.488 to -.029
Negative affect	-.416	-.416**	-.502 to -.330	Negative affect	-.556	-.556**	-.682 to -.430
Overall: $R^2 = 0.37$ , $F(11,417) = 21.9^{**}$				Overall: $R^2 = 0.47$ , $F(11,194) = 15.0^{**}$			

\* $< 0.05$ , \*\* $< 0.001$

$\beta$  = standardised regression coefficient; B = unstandardised regression coefficient; 95% C.I. = confidence interval for B. Additional covariates included in the model were not significant predictors of positive affect: age, sex rank, years as a pilot, physical inactivity, alcohol misuse, objective work index

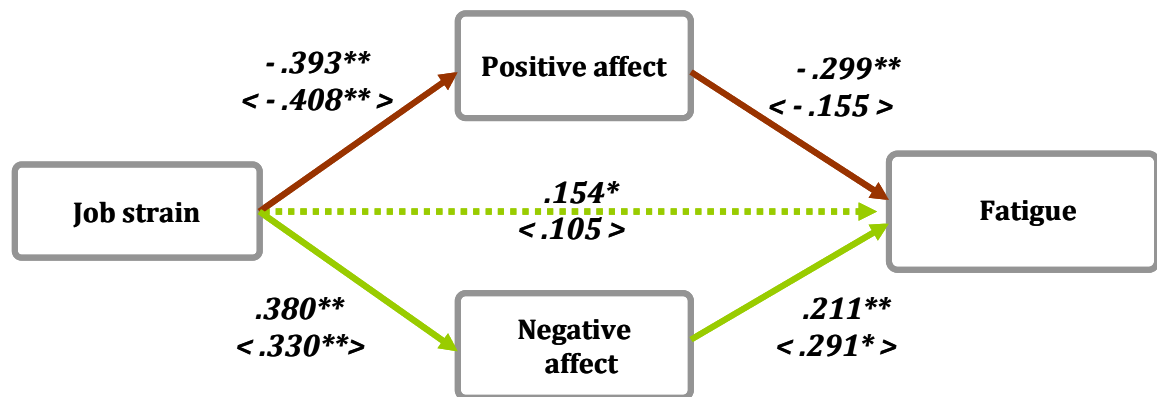
### 5.3.2 Hypothesis 2: PA & NA will mediate job strain to health associations

#### 1. Fatigue (*Fatigue Severity Scale*)

2010 In a simple linear regression model, job strain was significantly associated with fatigue ( $B = 0.369$ , 95% C.I. 0.280 to 0.459,  $R^2 = 0.136$ ). In multivariable analysis, with positive and negative affect included as covariates, all three variables independently predicted fatigue (job strain  $B = 0.149$ , positive affect  $B = -0.298$ , negative affect  $B = 0.224$ ; all  $p < 0.003$ ). The reduction in the job strain coefficient and significant main effects of all three variables indicated that both affect variables could be mediators of the association between job strain and fatigue. The  $R^2$  for this model was 0.298.

To confirm potential mediation pathways using PROCESS, positive and negative affect were inputted as mediators of the association between job strain and fatigue. Job strain had a significant direct effect on fatigue (effect size 0.15; 95% C.I. 0.06 to 0.25) and also a significant indirect effect, mediated by both positive affect (effect size 0.13, C.I. 0.09 to 0.18) and negative affect (effect size 0.09, C.I. 0.06 to 0.14). The combined indirect effect via positive and negative affect was therefore larger than direct effect from job strain to fatigue (0.15 direct, 0.22 indirect). When objective work index, demographics and health behaviours were included as covariates, job strain still predicted fatigue via both direct and indirect pathways and there was little change to the effect sizes (positive affect 0.12, C.I. 0.08 to 0.18; negative affect 0.08, C.I. 0.05 to 0.13). Regression coefficients for the adjusted model are illustrated in Figure 5.3. The model accounted for 32% of the variance in fatigue. Social support was also tested as a covariate but it did not have an independent association with fatigue ( $B = 0.001$ ,  $p = 0.983$ ) and there was no improvement to model fit.

**Figure 5.3 Positive and negative affect as mediators of the job strain and fatigue association**  
 Values are un-standardised regression coefficients for 2010, <2012 in brackets>, using PROCESS (Hayes 2013). Covariates included: work index, age, rank, years as pilot, diet, alcohol misuse, inactivity, smoking. \*\*p<0.001, \*p<0.05.



*2012* Linear regression results were very similar to 2010. The regression coefficient for job strain predicting fatigue reduced from  $B = 0.331$  (95% C.I. 0.197 to 0.465) to  $B = 0.147$  (C.I. 0.060 to 0.288) with the addition of positive and negative affect. In PROCESS, based on the smaller sample size, the direct relationship between job strain and fatigue was no longer significant when mediators were introduced to the model (effect size 0.11, C.I. -0.02 to 0.26,  $p = 0.09$ ). In the model adjusted for covariates, both mediators retained significant indirect effects (positive affect 0.06, 95% C.I. 0.002 to 0.14; negative affect 0.09, C.I. 0.03 to 0.19). The mediation effect for positive affect remained significant despite the fact that the regression coefficient from positive affect to fatigue was not significant in the adjusted model ( $B = -0.155$ , C.I. -0.318 to 0.009,  $p = 0.06$ ) (Figure 5.3).

## 2. Sleep problems (Jenkins Sleep Scale)

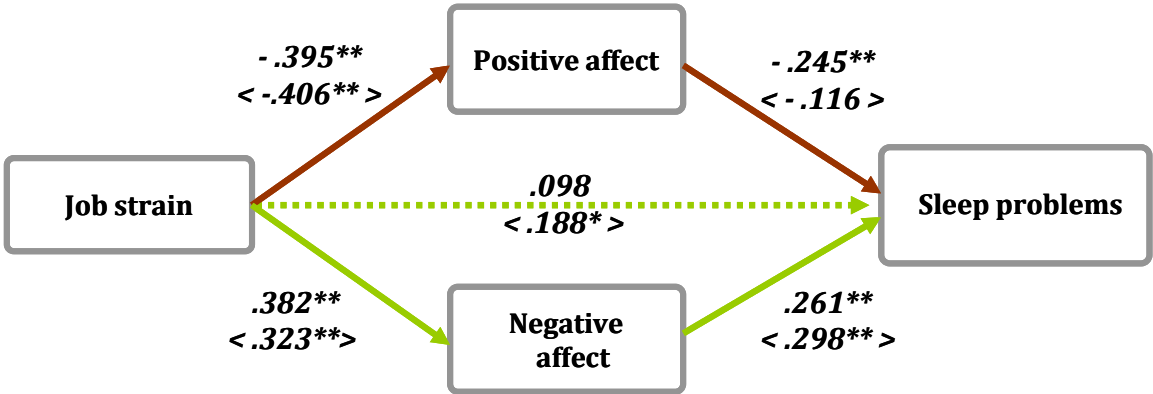
*2010* Job strain predicted sleep problems in simple linear regression ( $B = 0.314$ , 95% C.I. 0.222 to 0.405,  $R^2 = 0.098$ ). When positive and negative affect were added, all three variables predicted sleep problems (job strain  $B = 0.097$ , positive affect  $B = -0.250$ , negative affect  $B = 0.267$ ; all  $p < 0.05$ ). Model  $R^2$  increased to 0.256. Mediation effects were confirmed using PROCESS. Job strain had both a direct effect on sleep problems (effect size 0.10, C.I. 0.007 to 0.19) and indirect effects via positive affect (effect size 0.10, C.I. 0.06 to 0.16) and negative affect (effect size 0.11, C.I. 0.07 to 0.16). After adjustment for covariates, the direct effect of job strain on sleep problems was of borderline significance ( $p = 0.051$ ) but there was little change to the effect sizes. Indirect pathways via positive affect (effect size 0.10, C.I. 0.05 to 0.15) and



negative affect (effect size 0.10, C.I. 0.05 to 0.15) were of similar magnitude (Figure 5.4). The model accounted for 27% of the variance in sleep problems. Social support was not associated with sleep problems when added as a covariate ( $B = 0.004$ ,  $p = 0.928$ ).

**Figure 5.4 Positive and negative affect as mediators of the job strain and sleep problems association**

Values are un-standardised regression coefficients for 2010, <2012 in brackets>, using PROCESS (Hayes 2013). Covariates included: work index, age, rank, years as pilot, diet, alcohol misuse, inactivity, smoking. \*\* $p < 0.001$ , \* $p < 0.05$ .



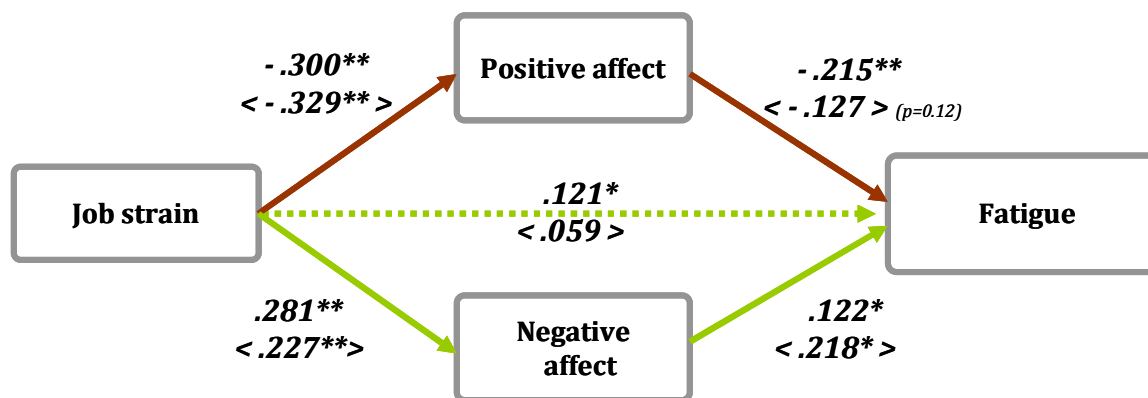
*2012* In linear regression, job strain predicted sleep problems ( $B = 0.310$ , C.I. 0.175 to 0.445) but when positive and negative affect were added to the model, only job strain ( $B = 0.175$ , C.I. 0.027 to 0.323) and negative affect ( $B = 0.229$ , C.I. 0.058 to 0.400) significantly predicted sleep problems. Positive affect had an inverse association with fatigue but was not a significant predictor ( $B = -0.097$ , C.I. -0.272 to 0.078). Similarly, in PROCESS models, direct effects of job strain and indirect effects via negative affect were statistically significant. Effect sizes for the fully adjusted model were: job strain (0.18, C.I. 0.04 to 0.33), negative affect (effect size 0.10, C.I. 0.04 to 0.18), positive affect (effect size 0.05, C.I. -0.03 to 0.13). Regression coefficients are shown in Figure 5.4.

*Post hoc analysis: sleep problems as a predictor of fatigue*

Hypothesis 2 was based on sleep problems and fatigue as separate outcomes, but sleep problems are also known to contribute to fatigue (Tham et al., 2013) and both outcomes were positively correlated (Table 5.2). To test whether job strain, positive and negative affect had significant associations with fatigue after taking sleep problems into account, I re-tested the model to predict fatigue (Figure 5.3) including sleep problems as a covariate. In 2010, all three

direct and indirect pathways from job strain to fatigue remained statistically significant, though the effect sizes were reduced (job strain direct from 0.15 to 0.12, via positive affect from 0.12 to 0.06, via negative affect from 0.08 to 0.04 (Figure 5.5). Sleep problems also had an independent association with fatigue in this model ( $B = 0.342$ , C.I. 0.254 to 0.430). Model  $R^2$  increased from 0.322 to 0.408. In 2012, with the smaller sample size, only negative affect and sleep problems had a significant association with fatigue in the fully adjusted model.

**Figure 5.5** Positive and negative affect as mediators of the job strain and fatigue association after adjustment for sleep problems, work index, age, rank, years as pilot, diet, alcohol misuse, inactivity, smoking. \*\* $p < 0.001$ , \* $p < 0.05$ .



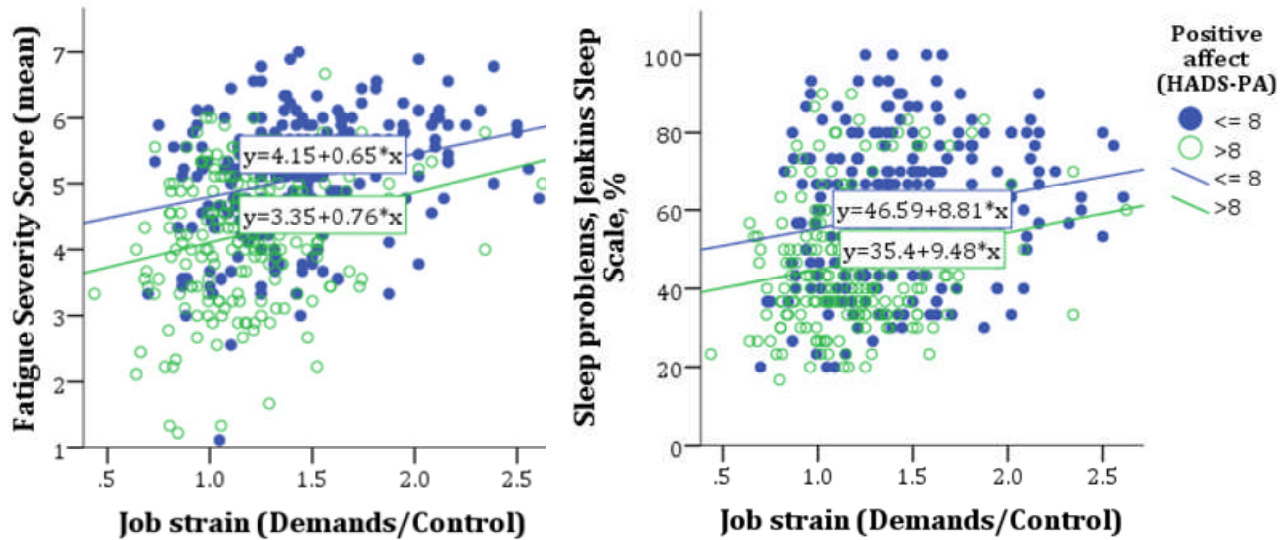
### 5.3.3 Hypothesis 3: PA as a moderator of the strain to health outcome association

Interaction terms for job strain x positive affect (PA\*strain) and job strain x negative affect (NA\*strain) were included as predictors in regression model to predict fatigue, adjusted for job strain, positive affect and negative affect. Neither interaction term significantly predicted fatigue in 2010 or 2012 (for 2010: PA\*strain  $B = -0.114$ , C.I. -0.185 to 0.413; NA\*strain  $B = -0.404$ , C.I. -0.866 to 0.060). Positive affect did not significantly moderate the association between job strain and fatigue. This is reflected in Figure 5.6 which shows regression lines for individuals high in positive affect (green circle outlines) and low in positive affect (blue filled circles) in 2010; regression coefficients differed by 16%.

In linear regression to predict sleep problems, interaction terms had no significant effects in 2010 or 2012, after adjustment for job strain, positive affect and negative affect (for 2010: PA\*strain  $B = 0.124$ , C.I. -0.186 to 0.434; NA\*strain  $B = -0.180$ , C.I. -0.658 to 0.298).

Figure 5.5 illustrates the regression lines for individuals high and low in positive affect in 2010; regression coefficients varied by only 7.3%, confirming that positive affect did not significantly moderate the association between job strain and sleep problems.

**Figure 5.6 Regression lines for the association between job strain and i) fatigue and ii) sleep problems**  
Individuals high in positive affect (green circles) vs. low in positive affect (blue filled circles) in 2010



## 5.4 Conclusions

This study showed that in two cross-sectional workforce surveys, job strain was consistently associated with low positive affect and high negative affect. These associations were independent of objective work history, demographic and behavioural characteristics. Positive and negative affect explained approximately 60% of the association between job strain and fatigue and 69% of the association between job strain and sleep problems – a substantial effect. Exploratory mediation analyses suggested that both positive and negative affect may mediate the association between job strain and health outcomes. Indirect pathways via affect were stronger than the direct pathway from job strain to fatigue or sleep problems. Positive affect did not appear to be a moderator of the relationship between job strain and fatigue or sleep problems.

These analyses support the hypothesis that experiencing a work environment associated with high psychological demands and low control may lead to fewer opportunities to experience positive emotions, in addition to greater negative emotion. It has been established by prospective studies that job strain increases the risk of negative mood disorders, such as anxiety and depression (Stansfeld et al., 2008; Stansfeld et al., 2012). Adverse psychosocial working conditions characterised by high demands and low control may also limit the opportunities to build psychosocial resources such as mastery, autonomy and social relatedness, which are necessary for positive psychological well-being (Ryan and Deci, 2000). A longitudinal study by Armon et al. (2012) indicated that low control and high demands predicted decreased vigour after four years, after adjusting for neuroticism. Effects from job conditions to vigour were stronger than the association from vigour to work stress, although bidirectional associations were observed.

Exploratory mediation analyses suggested that positive and negative affect could mediate the relationship between job strain and sleep problems, and with fatigue, independently of lifestyle behaviours. Indirect effects via positive and negative affect were stronger and more consistent than direct effects and were independent of social support. Results were of a similar magnitude for both health outcomes and within two surveys, completed two years apart. The review of psychobiological pathways in Chapter 2 (sections 2.2.2 and 2.2.3) suggested that high positive affect and low negative affect are associated with lower cardiovascular arousal and mean cortisol release during the day. Literature reviewed in 2.2.4 also identified links between positive affect and an impaired immune response, raised inflammatory markers and a less healthy metabolic profile. The study in Chapter 3 confirmed an association between positive affect and enhanced biological recovery from acute stressors. Individuals who experience a reduction in positive affect (and/or an increase in negative affect) as a consequence of job strain may therefore have higher chronic physiological arousal and a higher chronic allostatic load (Chandola et al., 2008), which might also lead to sleep problems and feelings of mental and physical fatigue.

This study reinforces the research showing that positive and negative affect, although inversely correlated, also have distinct correlates (Pressman and Cohen, 2005). Independent associations between job strain and positive and negative affect could have implications for

interventions to prevent or treat work stress. Workplace stress management interventions typically attempt to change work exposures at the organisational level or to provide individuals with practical techniques for coping with intense demands (such as time management) (Semmer, 2010). This study raises the possibility that promoting general well-being and increasing positive affect might influence more favourable perceptions of the psychosocial work environment, independent of attempts to reduce anxiety or negative emotions. Interventions to promote well-being and reduce job strain will be discussed further in Chapters 7 and 8.

Based on previously reported longitudinal research, I modelled pathways from job strain exposures to sleep and fatigue, rather than vice versa (Burgard and Ailshire, 2009; de Lange et al., 2009). However, in this cross-sectional analysis, reciprocal relationships from health outcomes to perceptions of job strain, directly or via changes in affect, cannot be ruled out. For example, Karlson et al. (2013) modelled the associations between insomnia symptoms and subjective and eudemonic well-being measured on three occasions over 10 years in over 4,000 adults. Recurrent insomnia symptoms were detrimental to both types of well-being at follow-up. It could also be that there is an affective component to perceptions of job strain. Individuals with a positive emotional style might perceive the same work demands as less of a burden than someone with a more negative outlook, or may identify more opportunities to exert individual control. There has been little prospective research examining the relationship between dispositional characteristics and job strain. Research based on the Cardiovascular Risk in Young Finns study found that the temperament traits of negative emotionality and lower sociability in 1992 predicted higher job strain and ERI 15-years later, aged 30-45 years (Hintsanen et al., 2011). There were no measures of objective work demands in the Finnish study and the authors suggested that temperament may influence occupational choices and how the environment responds to the individual, as well as perceptions of job strain. Importantly, in the current study, all participants shared the same occupation with similar physical working conditions. Job strain was associated with positive affect even after accounting for objective work history, reinforcing the importance of individual variation in affective experience and perceptions of the work environment. Longitudinal studies with repeated measures of exposures, affect and health outcomes over time would be preferable to confirm the temporal relationships between variables.

In addition to the limitations inherent in the interpretation of cross-sectional data, another important limitation of this study was the reliance on two related self-reported health outcomes. Sleep problems and fatigue were closely related but exploratory post hoc analysis showed that positive and negative affect were still associated with fatigue after co-varying for sleep problems in 2010, indicating that these were partially independent outcomes. Analyses of other outcomes, such as self-rated health or physical symptoms, may have reinforced these findings. However all pilots were screened for serious health conditions so it is probable that sleep problems and fatigue were the most prevalent adverse outcomes. When psychosocial predictors and health outcomes are both assessed via self-reports, they share common method variance, and which can lead to inflated associations (Podsakoff et al., 2003). One study used an Actiwatch sleep activity monitor to demonstrate that trait positive affect predicted better objective sleep quality over 8 days, consistent with the inverse association between positive affect and self-reported sleep problems in this study (Ong et al., 2013). Self-reported sleep problems and fatigue have been shown to predict cardiovascular disease in healthy cohorts, reinforcing the potential prognostic relevance of these outcomes (Hoevenaars-Blom et al., 2011; Ekmann et al., 2012).

This study was conducted within a relatively homogenous sample of pilots working full-time for a single airline. This offered advantages in terms of the availability of accurate records of physical work history, but the findings may not generalise to other occupations. Approximately 41% of the eligible population of BALPA pilots responded to the postal survey in 2010, but only 17% responded in 2012, owing to difficulties with reaching BALPA members via email. It is possible that only those with higher levels of fatigue or dissatisfied with their jobs were motivated to participate; survey respondents reported high levels of fatigue and sleep problems compared with other general population samples. It was reassuring that given the lower participation rate in 2012, the hypothesised associations between job strain and positive affect, and job strain and health outcomes, were of a similar magnitude in both surveys. Mediation effects from job strain to sleep problems via positive affect were not statistically significant in 2012, but the analysis may not have been powered to detect significant changes. Similarly there was no evidence to support a moderation effect in this study, but positive affect was based on a retrospective measure of positive affect over the last two weeks which was strongly inversely correlated with job strain. It is possible that a more

stable measure of dispositional positive affect or eudemonic well-being might have had a weaker direct association with job strain and a stronger moderation effect.

It was interesting that objective work history was less strongly associated with fatigue than job strain. Previous research investigating predictors of fatigue in airline pilots has concentrated on comparing the effects of different flight and shift patterns (Jackson and Earl, 2006; Powell et al., 2007; Spencer and Robertson, 2007). This study suggests that psychosocial perceptions of job strain explain at least 13% of the variance in fatigue in airline pilots. Theoretical bio-mathematical models to design work rosters to avoid fatigue are traditionally based on timing of sleep and working hours only; predictive models in pilots might be improved by the consideration of psychosocial exposures (Dawson et al., 2011).

In conclusion, this cross-sectional study found that job strain was associated with low positive affect, independently of objective work history, demographic and behavioural characteristics and negative affect. The findings suggest that positive and negative affect may each mediate the association between job strain and fatigue, and between job strain and sleep problems, but reverse associations cannot be ruled out. Longitudinal studies which investigate the relationships between job strain and health outcomes could examine the potential for independent influences of positive and negative affect on downstream biological processes. If such pathways can be demonstrated in longitudinal studies, it is possible that both increasing positive affect and reducing negative affect may be complimentary targets for interventions to prevent or alleviate job strain and its consequences.

## **Chapter 6 Job strain, positive affect and the diurnal cortisol rhythm on early shifts, late shifts and rest days in male pilots**

In Chapter 5, I found that job strain was associated with low positive affect, independently of negative affect. I suggested that a reduction in the daily experience of positive emotions and associated physiological activation could be one pathway linking job strain to sleep difficulties and fatigue. In this chapter, I investigate links between job strain, positive affect and cortisol, as an objective marker of neuroendocrine activity. In Chapter 2, I discussed the weak evidence for an association between positive affect and low cortisol over the day. In Chapter 4, I reviewed the literature linking job strain to diurnal cortisol. There appeared to be a relatively consistent association between job strain and raised evening cortisol, but the review highlighted inconsistencies and methodological limitations. In Chapter 6, I aim to address some of the methodological weaknesses of previous studies by examining the association between job strain and the diurnal cortisol rhythm over six days across different work shift conditions. I also explore whether associations between job strain and cortisol are related to experienced positive affect over the day. An article based on this study has been published in *Psychoneuroendocrinology* (Bostock and Steptoe, 2013).

### **6.1 Introduction**

Dysregulation of the HPA axis is one of the biological mechanisms that has been hypothesised to contribute to the increased risk of CVD associated with job strain (Chandola et al., 2008). Salivary cortisol is widely used as an indicator of activity of HPA axis function in large-scale epidemiological studies (Adam and Kumari, 2009), yet the evidence linking job strain and cortisol remains inconclusive (Chapter 4). In this study I address some of the most important methodological weaknesses identified in earlier studies: too few cortisol measurements, failure to consider the influence of different work shifts and leisure days, inaccurate measurement of the diurnal slope and neglect of potential confounders, such as smoking, sleep duration and quality.



Design of a cortisol salivary sampling protocol usually necessitates a compromise between the scientific rationale for large numbers of samples over multiple days (to account for within-person variability) and the practical constraints for participants of collecting and storing multiple samples. Too intensive a sampling protocol may act as a deterrent to participation and might even act as a 'stressful' event in itself, potentially interfering with the normal diurnal rhythm (Peeters et al., 2003). A minimum protocol of three samples on one day, including waking, post-waking and evening (or bedtime), can be used to calculate the awakening increase (CARi) and to derive a simple measure of diurnal decline (Bouma et al., 2009), but this does not allow an assessment of the curvilinear nature of the decline over the day. Analysis of the Whitehall II study, based on six samples on a single day from waking to bedtime, showed that both a flatter diurnal curve and a higher sample at bedtime were associated with increased all-cause and cardiovascular mortality (Kumari et al., 2011). Greater frequency of sampling over the day also enables more accurate assessment of daily total output, or area under the curve (AUC). For example, one study found that the AUC derived from 15 samples over 3 days had a correlation of 0.69 with the AUC derived from a minimal 3-sample protocol, a moderately strong association (Harville et al., 2007).

A two day sampling protocol in a sub-sample of the Whitehall II cohort showed that the CARi on a working day was higher than a weekend day (Kunz-Ebrecht et al., 2004a). Studies should therefore specify work and/or rest conditions when making between-subject comparisons. In the literature review in section 4.2.2, three of the 11 studies which assessed the association between job strain and the CAR failed to specify whether sampling was completed on a work or rest day. Effects that generalise across work and leisure days may be more likely to reflect stable trait rather than state differences. Rystedt et al. (2008) found that iso-strain was associated with higher evening cortisol on both work and rest days over a 7-day protocol. Rystedt argued that trait differences in evening cortisol may have more relevance for long-term health than differences in the CARi, which had less consistent associations with job strain. It has been suggested that a single day of saliva sampling is more likely to reveal state rather than trait factors associated with the CAR (Hellhammer et al., 2007).

In addition to specifying work and/or rest days, a cortisol sampling protocol should consider the timing of work shifts. In industrialised countries, almost one in five workers participates in shift work, in which different groups of workers replace each other in the same role (ILO, 2004). Night shift work severely disrupts the endogenous sleep-wake cycle and is associated with marked alterations to the diurnal cortisol rhythm (Scheer et al., 2009; Griefahn and Robens, 2010). The majority of studies testing the association between job strain and cortisol reviewed in Chapter 4 specified day workers but there is evidence that even waking a few hours early to start a daytime work shift might alter the diurnal rhythm. A previous study from our group showed that the same workers waking for an early shift (mean waking time 0400h  $\pm$  41 minutes) had a higher CARi than on later day shifts (waking time 0739h  $\pm$  94 minutes) or rest days (waking time 0804h  $\pm$  78 minutes) (Williams et al., 2005). A similar study using a within-subject design in nurses found that early shifts were associated with a higher CARi than afternoon or night shifts (Federenko et al., 2004). Despite these findings, several large studies have found no associated time of waking and the awakening response (Pruessner et al., 1997; Wust et al., 2000; Kunz-Ebrecht et al., 2004b). It has been suggested that early shift effects on the awakening response might be attributed to a more acutely stressful start to the day, rather than the time of waking, but this issue has not been widely explored (Williams et al., 2005). Inconsistency in the literature about the influence of time of waking or early shift work suggests that there may be an advantage in standardising work shifts in order to make valid between-subject comparisons of the diurnal rhythm between high and low job strain groups. Time of waking and acute stress should also be taken into account as potential confounders in the association between job strain and the CAR.

The review in section 4.2.2 suggested that job strain is related to increased evening cortisol (based on four out of five studies) implicating prolonged activation of the HPA axis over the day. Conversely, only one out of five studies reported an association between job strain and the diurnal decline. However, none of the studies in the review used more than two samples to measure the slope of decline over the day. Thomas et al. (2009) did not collect an evening sample and all four remaining studies calculated the diurnal decline as a simple a difference score from morning to evening (Steptoe et al., 2000a; Sjogren et al., 2006; Harris et al., 2007; Karlson et al., 2011). Crucially the difference score does not measure of the rate of decline over time, which differs depending on times of waking and bedtime. Studies by

Karlson (2007) and Harris (2007) also used the post-waking peak as the morning baseline level, as opposed to waking. It has been argued that the slope should be measured from waking since the awakening response is thought to be controlled independently from the diurnal decline (Clow et al., 2004).

In the current study, non-smoking pilots working a standardised rotating shift pattern collected 6 saliva samples over the day on a total of 6 days: 2 consecutive early shift days, 2 consecutive late shift days and 2 consecutive rest days. Six samples were collected at timed intervals each day including waking, 30 minutes post-waking and bedtime. This protocol enabled tests of the association between job strain and key indicators of the diurnal rhythm: the CARi, diurnal slope based on average rate of decline, bedtime level and AUC over the day. Sleep duration and sleep difficulties, which have been linked to a flatter cortisol rhythm and a higher CARi (Kumari et al., 2009), were recorded on each sampling day and tested as covariates in the analyses. Each cortisol sample after waking was accompanied by ratings of happiness, as a measure of positive affect, and stress, as an indicator of negative affect. This repeated measurement approach enabled tests of the associations between job strain and daily positive affect within each shift condition, and with overall mean positive affect which was based on the average of all affect ratings across 6 days. Steptoe et al. (2008a) previously found that positive affect based on 4 happiness ratings over one day and evening predicted lower mean cortisol on the same day. I hypothesised, based on the review in Chapter 4, that job strain would be associated with higher bedtime cortisol and a flatter diurnal rhythm. I also expected job strain to predict lower happiness ratings over the day, independent of negative affect. I expected that low positive affect would partly explain the association between job strain and raised cortisol.

### **6.1.1 Hypotheses**

Hypotheses 1 and 2 were informed by the review of the literature in section 4.2.2 which suggested that job strain had a relatively consistent association with raised evening cortisol, suggestive of a flatter diurnal decline. Hypotheses 3 and 4 were based on the associations between job strain and positive affect observed in Chapter 5.

- Hypothesis 1: The CARi will be higher on early shift days than late shift or rest days.

- Hypothesis 2: Job strain will be associated with higher bedtime cortisol and a flatter diurnal cortisol slope over the day, regardless of shift condition.
- Hypothesis 3: Higher job strain will be associated with lower positive affect, independent of negative affect.
- Hypothesis 4: Positive affect will partly explain associations between job strain and raised bedtime cortisol and a flatter slope, independent of negative affect (hypotheses 2,3 and 4 would indicate a mediation effect of positive affect on bedtime cortisol and the diurnal slope).

As discussed within sections 2.2.3, inconsistent associations between positive affect and the CARi and mean cortisol output over the day have also been reported in studies which have not controlled for the effects of shift work. Similarly, as described in section 4.2.2, job strain has been linked to a raised CARi and daytime cortisol, but conflicting associations have been published. I therefore reported associations between both positive affect and job strain with the CARi and AUCg, in addition to the hypothesised relationships.

## **6.2 Methods**

### *Participants*

Participants were healthy working pilots employed by the same low-cost commercial airline studied in Chapter 5. An invitation to participate in a research study to explore workplace cortisol levels was included in a newsletter emailed to BALPA members based in the UK in March 2011. Only male, non-smoking, full-time pilots were eligible to participate, to avoid the influence of gender and smoking on cortisol (Adam and Kumari, 2009). Pilots routinely taking steroid medication were excluded. All participants worked on the standardised shift pattern, consisting of 5 early shifts, followed by 3 rest (non-working) days, 5 late shifts and 4 rest days (5-3-5-4 pattern). Early shifts required the pilot to start work before 0600h and late shifts after 1200h, followed by 7-12 hours on duty. Pilots typically flew 2 or 4 flights per day, of between 45 minutes and 5 hours in length, returning home overnight. During the four weeks allocated for recruitment, thirty-six pilots volunteered to participate, of whom 30 were eligible. All 30 were sent detailed study information and gave written consent to participate. Sampling was completed between April and June 2011. The study was approved by the UCL

Research Ethics Committee. Copies of the participant information, logbook and questionnaire are included in the Appendix for Chapter 6.

**Figure 6.1 Study pack**  
Containing 36 Salivettes (6 per day) plus a logbook and study questionnaire

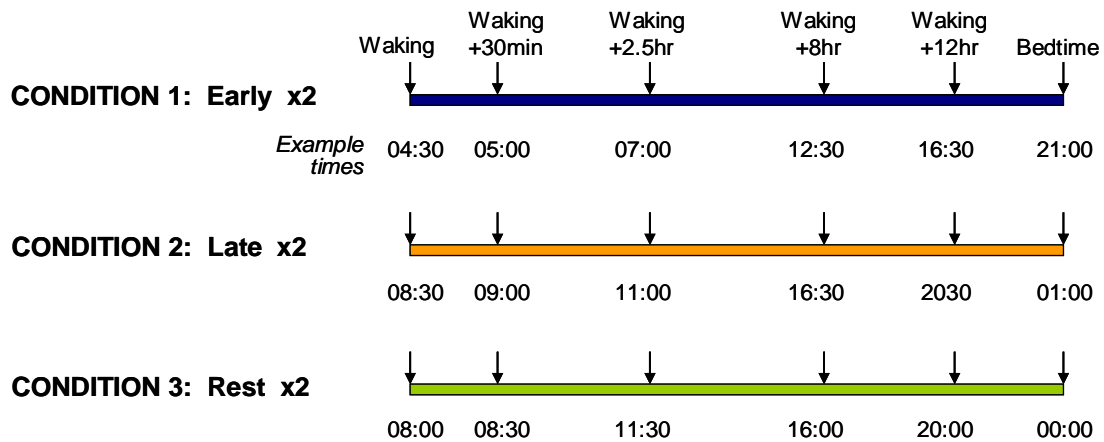


### *Cortisol procedure*

Participants received a sampling pack by post containing instructions, a questionnaire, a logbook and 36 labelled Salivettes (Sarstedt, Germany) (Figure 6.1). Participants collected saliva 6 times over the day on 2 consecutive days for each of 3 shift conditions: early shifts, late shifts and rest days. Although participants predominantly worked a 5-3-5-4 pattern, a computerised allocation system assigned occasional individual variations. To allow for this, participants were permitted to separate each 2-day sampling block by up to 10 days. An established sampling schedule was used capture the diurnal cortisol rhythm: waking (S1), waking +30m (S2), waking +2.5h (S3), waking +8h (S4), waking +12h (S5) and bedtime (S6) (Kumari et al., 2009). The sampling schedule is illustrated in Figure 6.2.

**Figure 6.2 Example saliva sampling schedule for the three conditions**

Pilots completed sampling for two consecutive days for each condition: early shifts, late shifts and rest days. Individual sampling times varied, depending on waking time.



Participants were asked to avoid eating, drinking caffeinated drinks or brushing their teeth for 15 minutes before each sample. At each sampling point after the waking sample pilots used the logbook to record the time and rated feelings of stress (as a measure of negative affect, NA) and happiness (positive affect, PA) over the previous 30 minutes. Moods were rated on a scale from '0' not at all to '4' extremely high. At the time of the first sample, participants recorded time of going to bed the previous night, time of waking and time of sample 1. Waking was defined as 'as soon as you open your eyes and while you are still in bed'. Bedtime was defined as 'the time at which you try to go to sleep'. As a measure of sleep quality, pilots were asked 'Did you sleep well last night?' with possible responses: '1' yes, I slept well, '2' quite well or '3' no, I did not sleep well. Participants recorded alcohol intake (yes / no) and whether or not they had completed 30 minutes exercise (yes / no) on each sampling day. On work days, pilots also recorded duty hours, flying hours and the number of sectors.

Salivettes were refrigerated and returned to the investigators by post. Salivary cortisol was measured using an enzyme-linked immunosorbent assay (ELISA) (SLV-2930, DRG International, Inc., USA) at the Technical University Dresden, Germany. The intra- and inter-assay coefficients of variation were less than 8%.

### *Measures*

Participants completed a short version of the 2010 employee survey described in section 5.2 and psychosocial work stress and fatigue were scored in the same way. Demographic measures were age, rank and years worked as a pilot. Psychosocial work environment was assessed using items from the Whitehall II Job Characteristics Questionnaire (Bosma et al., 1997), based on the Demand-Control model. Job strain was computed as a continuous measure of mean work demands (4-items) divided by mean job control (15-items). Separate scores for demands and control were converted to percentage scores for comparison with the previous studies (Chapter 5). To test for between-subject differences associated with job strain, scores were divided at the median into high and low groups. Fatigue was assessed using the 7-item Fatigue Severity Scale (Krupp et al., 1989; Lerdal et al., 2005).

### *Statistical Analysis*

Cortisol samples taken more than 15m from the timed protocol were excluded, including wake-up samples delayed >15m post awakening (Dockray et al., 2008). Extreme cortisol values ( $\geq \pm 3$  SD from the mean) were excluded. Paired t-tests were used to test for differences between pairs of samples at the same time point within each shift condition. There were no significant differences and values were all positively correlated so mean values were calculated for each time point within a shift condition. Cortisol results were skewed so logarithmic transformations were computed to improve the fit to a normal distribution. Analyses were carried out on transformed values, but raw data are presented in the figures. Where data were missing from one of the two days within a shift, data from the alternate day was used to maximise data availability. Cortisol values were incomplete for 3 participants; analyses are presented for 27 complete cases. The cortisol awakening response (CARi) was calculated as the mean increase between sample 1 (waking) and sample 2 (waking+30m). Cortisol output over the day (AUCg) was calculated using the trapezoid formula for area under the curve with respect to ground (Pruessner et al., 2003), based on all 6 samples. Diurnal slopes for each participant were calculated by regressing cortisol values on sample time using a piecewise approach to generate a mean rate of reduction in cortisol per hour. The slope was anchored on the waking sample and excluded the second (waking +30m) value (Cohen et al., 2006b).

Maximum sleep duration was estimated as the time between waking and bedtime the previous evening. Waking hours were calculated as the difference between recorded waking time and bedtime the same evening. Paired t-tests were used to test differences between duty hours, flying hours and sectors across early and late work shifts. Wilcoxon signed rank tests were used to test differences in the proportion of pilots smoking or exercising on each shift. Happiness (PA) and stress (NA) ratings at each time point within each shift condition were positively correlated so mean values for each time point within each shift condition were calculated. Mean PA and NA ratings were calculated for the same time point within each shift condition and also across all six days of sampling, described as the overall mean. Affect ratings were initially analysed with two-way repeated measures ANOVAs with shift condition (early, late, rest) and sample time (1-6) as within-subject factors. Differences in mean wake-up time, bedtime, waking hours, sleep duration, sleep quality, positive and negative affect by shift condition were assessed using repeated measures ANOVAs with shift condition (early, late, rest) as the within-subjects factor. Post hoc Bonferroni tests were used to identify significant differences between shifts.

*Hypothesis 1:* To test for within-person differences in diurnal cortisol between shifts, the CARi, AUCg, diurnal slope and bedtime sample were analysed with separate one-way repeated measures analyses of variance (ANOVA) with shift condition (early, late, rest) as the within-subject factor. To test whether waking time, duration of waking hours or sleep difficulties explained significant differences in diurnal cortisol between shifts, these factors were included as time-varying covariates in separate linear mixed models for each cortisol measure, using the mixed command in SPSS (UCLA, 2012).

*Hypothesis 2:* Correlations between cortisol, job strain and affect within each shift condition were examined using Pearson product-moment correlation coefficients. The influence of job strain on cortisol (CARi, AUCg, diurnal slope and bedtime sample) was tested using separate repeated measures ANOVAs with shift condition as the within-subjects factor, job strain (high/low, median split) as the between-subjects factor and age and rank as covariates (Van Cauter et al., 1996; Cohen et al., 2006b). Overall mean PA and NA were added to the model as covariates.

*Hypothesis 3:* The association between job strain and PA during each shift was tested in a repeated measures ANOVA with shift condition as the within-subjects factor, job strain



(high/low) as the between-subjects factor. The association between job strain (continuous) and overall mean PA was also tested in a regression model, adjusted for overall NA.

*Hypothesis 4:* Where between-subject differences in diurnal cortisol were identified by job strain in repeated measures ANOVAs, the robustness of these effects were further tested in linear mixed models in which mean values for each shift condition for time of waking, sleep duration, sleep difficulties, positive or negative affect were included as time-varying covariates. IBM SPSS Statistics version 21.0 was used for all statistical analyses.

### **6.3 Results**

#### *Participant characteristics*

Fourteen of the 27 participants were Captains and 13 were First Officers. The proportion of First Officers participating in this cortisol study was higher than the 2010 employee survey described in Chapter 5 (Table 6.1). The age and years of experience of pilots participating in these two studies were similar. Cortisol study participants had worked as a pilot for between 3 and 37 years. Perceptions of the work environment and fatigue did not differ significantly between the two pilot samples. Twenty-two out of 27 participants claimed to have completed the employee survey the previous year.

#### *Shift characteristics and differences between shifts*

Waking times ranged from 0340-0530h on an early shift, 0621-1225h on a late shift and 0641-0925h on a rest day. Early shifts were associated with significantly earlier waking, a longer waking day and shorter sleep duration than late shifts or rest days (Table 2). Bedtime was significantly later on a late shift. Sleep quality did not differ significantly between conditions. Objective work demands did not differ between work shifts. Drinking alcohol was more common on rest days.

**Table 6.1 Participant characteristics for the cortisol study**  
Comparison with the 2010 BALPA employee survey (described in section 5.3)

	Cortisol study % (n)	2010 Survey, full-time pilots %
<i>Rank</i>		
Captain	51.9 (14)	62.7
First officer	48.1 (13)*	27.3
<i>Age</i>		
20-29 years	14.8 (4)	12.4
30-39 years	40.7 (11)	39.0
40-49 years	29.6 (8)	35.6
50-64 years	14.8 (4)	12.9
Male	100 (27)*	96.2
Work full-time	100 (27)	100
Years as pilot, mean (SD)	12.7 (10.0)	13.6 (8.9)
Fatigue, mean (SD)	4.5 (1.0)	4.7 (1.0)
<i>Psychosocial work environment</i>		
Demands, mean % (SD)	66.7 (12.5)	70.1 (12.6)
Control, mean % (SD)	52.2 (9.4)	54.9 (9.0)
Job strain, mean (SD)	1.32 (0.38)	1.32 (0.37)
Social support, mean % (SD)	63.0 (15.3)	62.8 (17.5)
<i>Total n</i>	27	418

\*Sig. difference  $p < 0.05$ ; z-test to compare proportions, independent t-test for continuous variables

**Table 6.2 Mean shift characteristics on early shift, late shift and rest days**

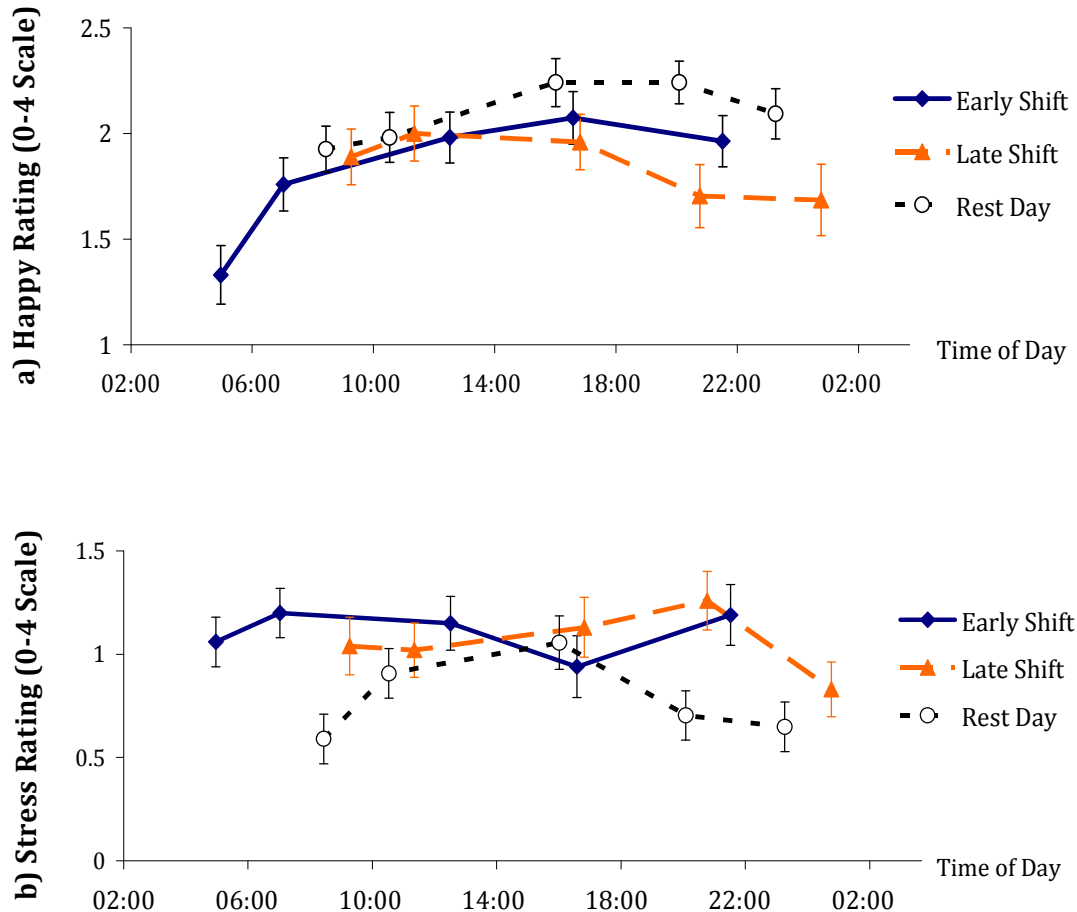
	Early shift	Late shift	Rest day
<i>Waking hours, sleep quality</i>			
Time of waking (h)	0426 ± 0023	0840 ± 0123 <sup>a</sup>	0752 ± 0100 <sup>a</sup>
Bed-time (h)	2131 ± 0043	0052 ± 0117 <sup>a,c</sup>	2316 ± 0042
Waking hours (h)	17.0 ± 0.8 <sup>b,c</sup>	16.1 ± 1.1	15.4 ± 1.0
Sleep duration (h)	7.0 ± 0.7	7.8 ± 1.4 <sup>a</sup>	8.2 ± 1.0 <sup>a</sup>
Poor sleep quality (1-3)	2.1 ± 0.6	1.9 ± 0.6	1.7 ± 0.6
<i>Work demands</i>			
Duty hours	8.0 ± 1.5	8.9 ± 1.6	-
Flying hours	5.4 ± 1.2	5.7 ± 1.4	-
Sectors (landings)	2.7 ± 0.7	2.9 ± 0.9	-
<i>Health behaviour</i>			
Alcohol consumed, y/n (%)	29.6	20.3	51.9 <sup>a,b</sup>
Exercised >10min, y/n (%)	20.4	16.7	27.8
<i>Mean affect over the day</i>			
Positive affect (0-4)	1.82 ± 0.5	1.86 ± 0.6	2.10 ± 0.4 <sup>a,b</sup>
Negative affect (0-4)	1.11 ± 0.5 <sup>c</sup>	1.06 ± 0.5 <sup>c</sup>	0.78 ± 0.4
<i>Cortisol, natural log</i>			
Increase on waking, CAR	0.83 ± 0.38 <sup>b,c</sup>	0.25 ± 0.41	0.35 ± 0.35
Diurnal slope	0.11 ± 0.06	0.15 ± 0.07 <sup>a</sup>	0.20 ± 0.18 <sup>a</sup>
Bedtime cortisol, S6	0.68 ± 0.64	0.98 ± 0.78 <sup>c</sup>	0.45 ± 0.92
Area under curve, AUC <sub>G</sub>	32.8 ± 6.80 <sup>b,c</sup>	26.4 ± 6.50	23.7 ± 7.29

Means ± standard deviation. <sup>a,b,c</sup> significantly higher than early<sup>a</sup>, late<sup>b</sup> and rest<sup>c</sup> days (p<0.05).

PA and NA over the day during each shift are illustrated in Figure 6.3. There were significant main effects of shift ( $F(2,52)=6.86$  and time ( $F(4,104)=4.94$ ,  $p=0.001$ ) on PA. There was a main effect of shift only on NA ( $F(2, 52)=5.80$ ,  $p=0.005$ ). Work shifts were associated with higher NA and lower PA than rest days (Table 6.2). There were significant shift-time interactions for both measures ( $F(8, 208)>2.73$ ,  $p>0.006$ ). Happiness ratings were at a low-point at the start of an early shift, but peaked on all days mid-afternoon. Stress ratings decreased at the bedtime sample on rest and late days, but peaked before bed on early shifts. Mean PA on an early shift correlated with PA on the late shift ( $r=0.79$ ,  $p<0.001$ ) and to a lesser extent PA on rest days ( $r=0.58$ ,  $p=0.002$ ). NA on early shifts was correlated with late shifts

( $r=0.42$ ,  $p=0.030$ ) but less closely related to rest days ( $r=0.30$ ,  $p=0.130$ ). Overall PA, derived from all happiness ratings over 6 days, was not significantly correlated with overall NA ( $r=0.27$ ,  $p=0.171$ ).

**Figure 6.3 Subjective mood ratings over the day for a) happiness (PA) and b) stress (NA) during each shift condition**

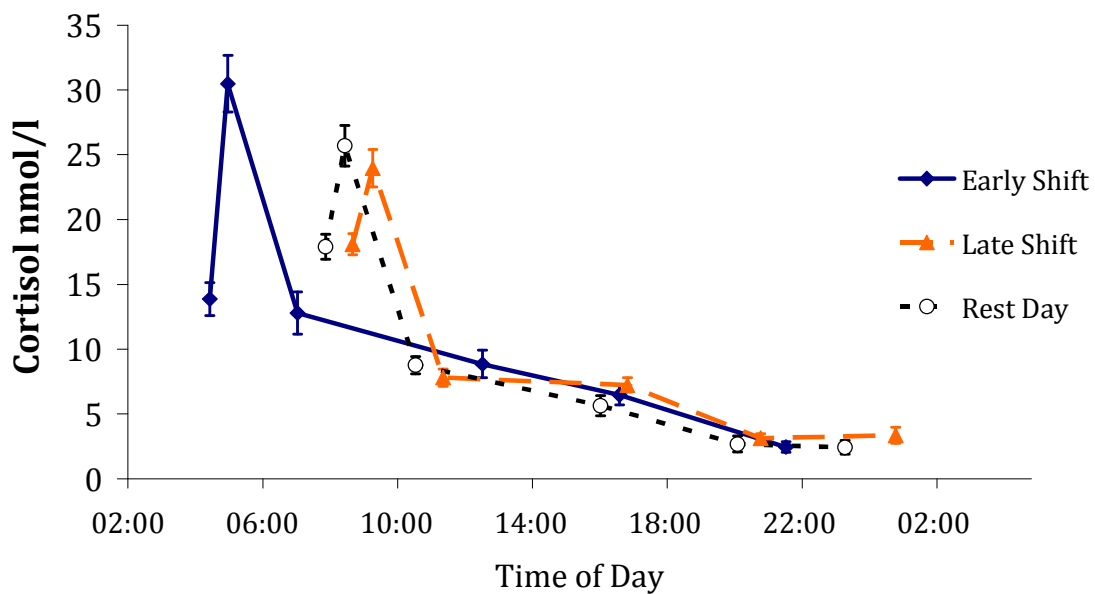


### 6.3.1 Hypothesis 1: CARi will be higher on early shifts

Diurnal cortisol patterns by shift condition are illustrated in Figure 6.4. In separate unadjusted repeated measures ANOVAs, there were main effects of shift on the CARi ( $F(2,52)=18.09$ ,  $p<0.001$ ), diurnal slope ( $F(2,52)=5.09$ ,  $p=0.024$ ), bedtime sample ( $F(2,52)=3.91$ ,  $p=0.026$ ) and total output over the day (AUCg) ( $F(2,52)=29.80$ ,  $p<0.001$ ). As hypothesised, the CARi was significantly higher on an early shift than on both late and rest days. This pattern was due to both a lower waking sample and a higher cortisol peak after 30

minutes. In addition, the total cortisol output over the day, AUCg, was higher and the diurnal slope was significantly lower, or flatter, on an early shift than a late shift or rest day. There were no significant differences in the CARi, diurnal slope or AUCg between a late shift and a rest day. The final cortisol sample of the day before sleeping, the bedtime sample, was significantly higher on a late shift than on a rest day only (Table 6.2).

**Figure 6.4** Diurnal cortisol release by shift condition for early shifts, late shifts and rest days  
Each data point is the mean value averaged across two consecutive days



Mean time of waking, duration of waking hours and sleep difficulties for each shift condition were introduced as time-varying covariates into separate repeated measures models for each cortisol indicator, with shift condition as the within-subjects factor. These covariates were not significantly associated with the CARi, AUCg or bedtime cortisol; shift differences in the CARi and AUCg persisted after adjustment for all three variables ( $F > 5.40$ ,  $p < 0.008$ ; both models). Waking hours significantly predicted diurnal slope ( $F = 7.08$ ,  $p = 0.009$ ). Longer waking hours (which corresponded to shorter sleep duration), were correlated with a smaller (flatter) diurnal slope on all three shift conditions (for example, on a rest day:  $r = -0.38$ ,  $p = 0.049$ ). After adjustment for waking hours, the effect of shift condition on diurnal slope was no longer statistically significant ( $F = 1.21$ ,  $p = 0.304$ ).

Several cortisol indicators were inter-correlated: a steeper mean diurnal slope was associated with a lower mean bedtime value ( $r = -0.74$ ,  $p < 0.001$ ) and lower total output, AUCg ( $r = -0.62$ ,  $p = 0.001$ ). AUCg was also positively correlated with the mean bedtime value ( $r = 0.83$ ,  $p < 0.001$ ). The mean CARi was not significantly associated with other cortisol indicators.

### 6.3.2 Hypothesis 2: Job strain will be associated raised bedtime cortisol

Table 6.3 lists bivariate correlations between aspects of the diurnal cortisol rhythm, job strain and affect ratings within each shift condition and mean values across conditions. These correlations are shown to give an indication of the direction of associations and variability across different shift conditions.

**Table 6.3 Correlations between the diurnal cortisol rhythm, mean positive and negative affect ratings over the day and job strain**  
Early shifts, late shifts, rest days and mean values across all three shift conditions

Cortisol, natural log	Job strain	Positive affect				Negative affect			
		Early	Late	Rest	Mean	Early	Late	Rest	Mean
CAR	Early	-.156	-.125		-.006	-.165			-.203
	Late	.321	-.376		-.474*		.135		.162
	Rest	.364		.058	-.048			.009	.111
	Mean	.304	-.343	-.220	-.317	-.326	.007	.015	.062
Diurnal slope	Early	-.166	-.195		-.153	.167			.076
	Late	-.316		0.394*	0.397*		-.016		.002
	Rest	-.333		.304	.219			-.146	-.134
	Mean	-.384*	.112	.200	.347	.240	.078	-.117	-.119
Bedtime	Early	.030	.238		.146	-.066			.108
	Late	.114		-.239	-.133		.322		.226
	Rest	.421*		-.219	-.133			.211	.244
	Mean	.274	.095	-.103	-.303	-.074	-.074	.380	.246
AUC <sub>G</sub>	Early	-.032	.251		.149	.013			.113
	Late	.009		-.129	-.068		.282		.301
	Rest	.334		-.089	-.040			.160	.214
	Mean	.130	.147	-.024	-.089	.016	.096	.284	.196
Job strain	1	-.235	-.191	-.093	-.0200	.159	.229	.015	.144

Pearson product-moment correlation coefficients. Mean values computed across all three shift conditions.

**Bold** highlights correlations  $> 0.325$  or  $< -0.325$  ( $p < 0.10$ ), \* $p < 0.05$

Job strain was correlated with a flatter diurnal slope on all three shift conditions, resulting in a significant inverse correlation with the mean slope value ( $r = -0.384$ ,  $p = 0.048$ ). There was a trend for job strain to be associated with higher bedtime cortisol, but this correlation was only significant on a rest day. The direction of associations between job strain and the CARi and AUCg were not consistent across shifts (Table 6.3).

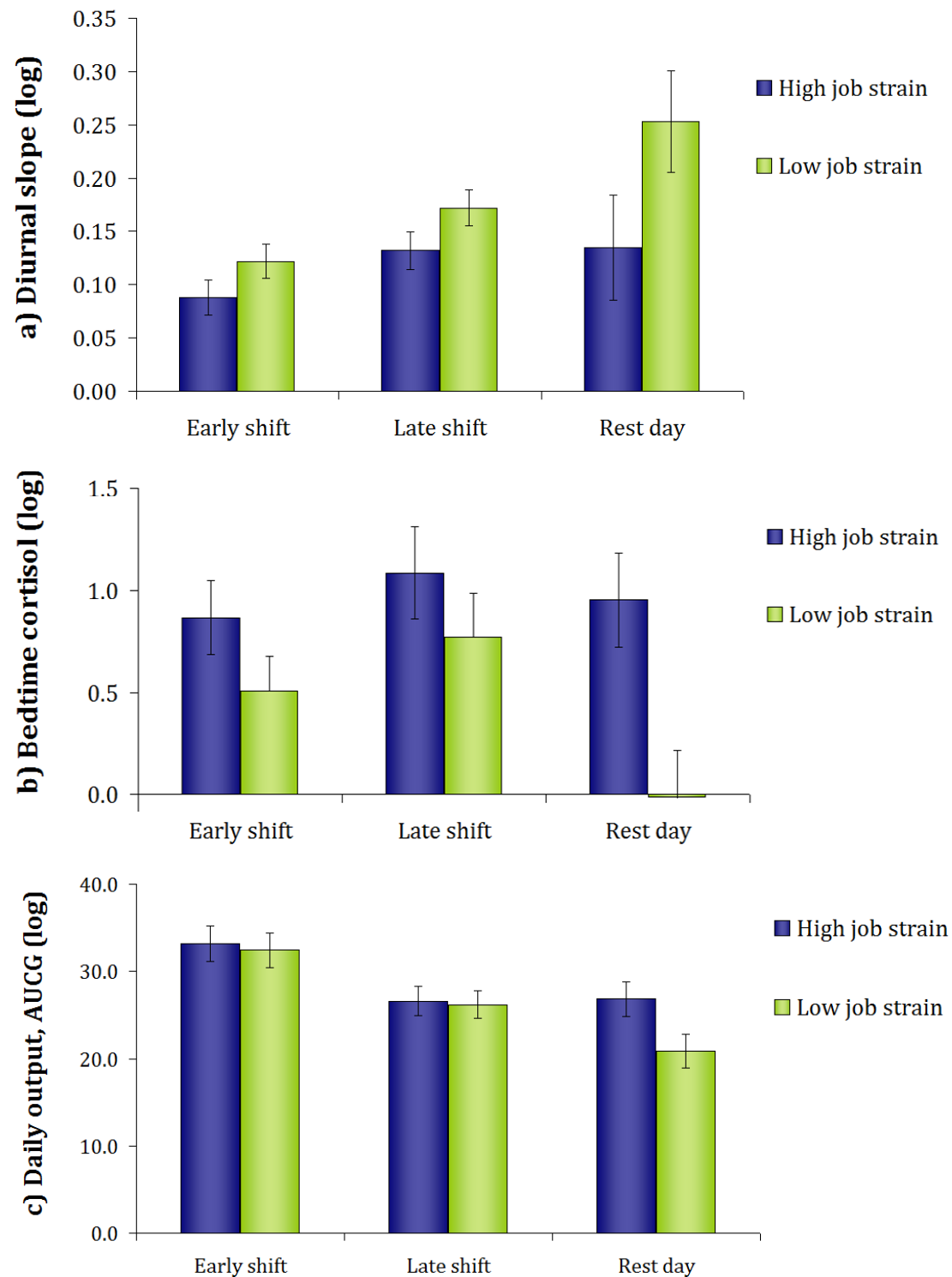
Separate repeated measures ANOVAs were calculated for each of the four cortisol measures with job strain (high/low) as the between-subjects factor and shift as the within-subjects factor, adjusted for age and rank. The F-statistics for the between-subjects effects of job strain are listed in Table 6.4 (model 1). High job strain was significantly associated with a smaller (flatter) diurnal decline and higher bedtime cortisol. These associations are illustrated in Figure 6.6a and 6.6b. There was no overall between-subjects effect of job strain on AUCg, but there was an interaction between shift and job strain ( $F = 3.57$ ,  $p = 0.037$ ): on a rest day only, the high strain group produced more cortisol over the day (Figure 6.6c). Job strain was not associated with waking cortisol, or peak cortisol.

**Table 6.4      Between-subjects effects of job strain on diurnal cortisol rhythm**  
Repeated measures ANOVAs with shift condition as the within-subjects factor, all models adjusted for age and rank

	F statistic			
	CARi	Slope	Bedtime	AUCg
Model 1. Job strain (High vs. low)	0.405	5.002*	6.531*	1.839
Model 2. Job strain (High vs. low), +adjusted for overall PA	0.285	4.601*	6.057*	1.648
Model 3. Job strain (High vs. low), +adjusted for overall NA	0.274	3.762	5.186*	1.249

Bold highlights associations approaching significance,  $p < 0.10$ ; \* $p < 0.05$ . Age and rank included as covariates in all models

**Figure 6.5** Associations between job strain (high/low) and a) diurnal slope, b) bedtime cortisol, c) AUCg on early shifts, late shifts and rest days adjusted for age and rank

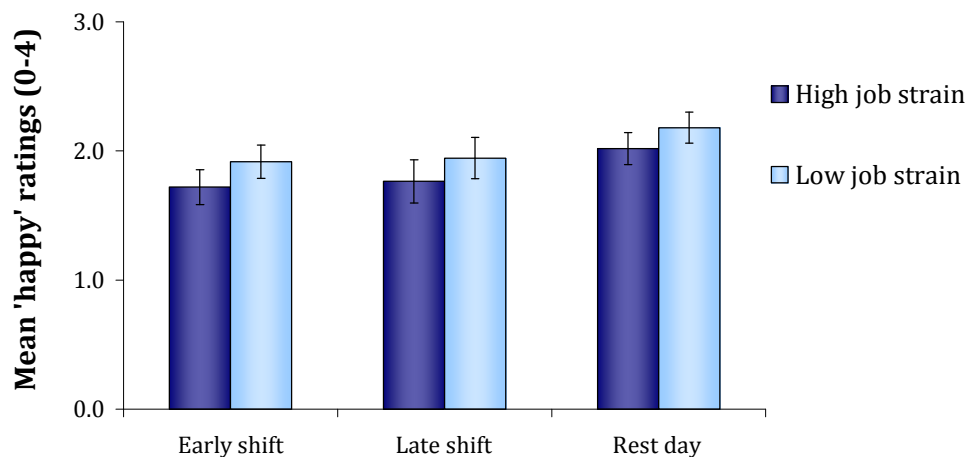




### 6.3.3 Hypothesis 3: Job strain will be associated low PA, independent of NA

As illustrated in Figure 6.5 below, there was a trend for individuals reporting high job strain to experience less PA over the day than individuals reporting low job strain. However, counter to hypothesis 3, in a repeated measures ANOVA for PA with binary job strain as the between-subjects factor and shift as the within-subjects factor, job strain was not significantly associated with PA across shifts, with or without adjustment for NA (adjusted  $F(1,25)=1.04$ ,  $p=0.318$ ). In a linear regression model to predict overall mean PA, neither job strain ( $B = -0.191$ , 95% C.I.  $-0.561$  to  $0.179$ ) nor mean NA ( $B = 0.361$ , C.I.  $-0.118$  to  $0.840$ ) were significantly associated with PA.

**Figure 6.6** Mean positive affect by job strain (high vs. low) on early shifts, late shifts and rest days, adjusted for negative affect



### 6.3.4 Hypothesis 4: PA will partly explain associations between job strain and cortisol, independent of negative affect

Counter to hypothesis 4, there were no significant correlations between PA ratings on a single shift condition and the total cortisol output, AUCg, within the same shift. There was a trend for overall PA to be associated with a lower CARi on all shift conditions, but the correlation was significant only on a late shift ( $r = -0.474$ ,  $p=0.013$ ). Overall mean PA was also associated with a steeper diurnal slope on a late shift ( $r = 0.397$ ,  $p=0.041$ ) and to a lesser extent a rest day ( $r = 0.219$ ,  $p=0.243$ ) but not on an early shift. NA ratings were not significantly correlated with

cortisol; trends for associations with higher bedtime cortisol and higher AUCg were not significant.

Overall PA was added as a covariate to the repeated measures ANOVAs for each cortisol indicator in which job strain was entered as a between subjects factor (Table 6.4, Model 2). There was no evidence to support hypothesis 4 or 5. Positive affect had no significant within- or between- subjects effects on AUCg or any other cortisol indicator. There was little change to the significant associations between job strain and the diurnal slope and bedtime cortisol. The association between job strain and slope was borderline statistically significant after additionally adding NA as a covariate ( $p=0.066$ ), but NA had no within- or between- subjects effects on cortisol.

Finally, associations between job strain and cortisol indicators were tested in linear mixed models with shift condition as the within-subjects factor, time of waking, sleep problems and waking hours as time-varying covariates and job strain as a continuous variable. Job strain was significantly associated with diurnal slope ( $F=9.12$ ,  $p=0.005$ ) and the association with bedtime cortisol was close to significance ( $F=3.35$ ,  $p=0.078$ ). Adjustment for objective work history, exercise or alcohol by shift did not alter these associations. In separate models with PA and NA ratings as time-varying covariates, job strain was still associated with a flatter diurnal slope ( $F=4.58$ ,  $p=0.041$ ). PA at shift level did not significantly predict the CARi ( $F=1.55$ ,  $p=0.219$ ), the diurnal slope ( $F=1.88$ ,  $p=0.174$ ), bedtime cortisol ( $F=0.548$ ,  $p=0.462$ ) or AUCg ( $F=0.252$ ,  $p=0.618$ ). NA had no independent associations with cortisol in any of these models.

### **6.3.5 Conclusions**

Early shift days, which involved waking before 0530h, were associated with a higher CARi, a flatter slope and a higher AUCg than rest or late shift days, even after adjusting for waking time. In this study job strain was associated with high bedtime cortisol levels and a flatter diurnal slope over the day. Associations between job strain and the diurnal rhythm were not explained by adjusting for type of work shift or rest day, waking time, sleep difficulties or duration, positive or negative affect. Correlations between positive affect and job strain, and between positive affect and cortisol, were weak and non-significant in this study.

As hypothesised, based on the review of literature in Chapter 4 (section 4.2.2), job strain was associated with raised bedtime cortisol levels and a flatter diurnal rhythm. These patterns were present on all three shift conditions, but were particularly marked on a rest day (Figure 6.6b). The consistent association between job strain and raised bedtime cortisol across shift conditions reinforces findings of the study by Rystedt et al. (2008) in which chronic iso-strain was associated with high 10pm cortisol levels on both work and weekend days. Aardal-Eriksson et al. (1998; 2001) showed that evening cortisol levels correlated positively with mental distress in both rescue workers and healthy adults nine months after a traumatic event, suggesting that prolonged exposure to a range of adverse psychosocial circumstances may be associated high evening cortisol. Importantly, associations in the current study were largely independent of positive and negative affect and sleep difficulties on the day of testing, suggesting that evening elevation is relatively insensitive to normal variation in psychological states. Failure for cortisol to decline to low evening levels might reflect an inability to physically ‘unwind’ at the end of the day or could reflect impaired central negative feedback sensitivity of the HPA axis, as has been described in obesity (Mattsson et al., 2009). Kumari et al. (2011) found that a flatter diurnal cortisol rhythm predicted cardiovascular mortality independently of behavioural covariates, hypertension, obesity, lipids, and fasting glucose, raising the prognostic significance of this marker.

There was no reliable association between job strain and daily output (AUCg) despite a significant association with high evening levels. Early shifts were significantly associated with greater AUCg during the day. A recent study showed that high 24-hour urinary cortisol output predicted cardiovascular mortality (Vogelzangs et al., 2010). Chronic over-secretion of cortisol in Cushing’s syndrome is associated with hyperglycaemia, insulin resistance and dyslipidaemia (Whitworth et al., 2005). Chronic exposure to heightened cortisol levels on early shifts, and potentially adverse metabolic consequences such as insulin resistance, could be a mechanism contributing to increased risks of heart disease in rotating shift workers (Fujino et al., 2006). Future research using 24-hour sampling methods could test whether the heightened evening cortisol levels associated with job strain correspond to higher cortisol release during sleep. There is a need for longitudinal studies to test the dynamics of chronic exposure to work stress and shift work and alterations in the diurnal rhythm, since in a cross-

sectional study such as this, we cannot rule out that those with higher evening cortisol levels and a flatter diurnal cortisol rhythm were more prone to experience work stress.

Counter to the findings of the meta-analysis by Chida and Steptoe (2009b), job strain was not reliably associated with the CARi in this sample. A striking feature of this study is the large within-individual variation in the diurnal cortisol rhythm by shift condition (Figure 6.4). Levels of positive affect were inversely correlated with the CARi on a late shift, and but the association was not significant in repeated measures analyses. Job strain had a weak positive correlation with the CARi on a late shift and a rest day but not on an early shift. It may be that the CARi is more influenced by psychological state or other biological parameters than other aspects of the diurnal rhythm. Williams et al. (2005), reported that ratings of stress at 30 minutes post waking explained differences in the CARi associated with different work shifts within transport workers. Shift differences in the CARi persisted after co-varying for stress and happiness in the current study but we did not capture anticipated stress (Fries et al., 2009). In a case study of one subject over 50 mornings, Stalder et al. (2010) reported that the awakening response was predicted by anticipated study day obligations or anticipated lack of leisure, but not by stress measured on the same day. Wide individual variability in the CARi was also reported in this case series (3.6-39.0nmol/l) (Stalder et al., 2009), raising questions about the reliability of 'normal' CARi values which do not specify work shift or rest days (Wust et al., 2000).

In this study, regardless of job strain, early shifts were associated with a higher CARi, a flatter diurnal slope and greater daily cortisol output than late shifts or rest days. The difference in diurnal slope was explained by longer waking hours but differences in the CARi and AUCg were not explained by waking time, sleep duration, sleep difficulties, objective work demands, exercise or alcohol. Two previous studies using a within-subject design in shift workers also found that waking for an early shift was associated with a higher CARi (Federenko et al., 2004; Williams et al., 2005). Kudiella et al. (2003) also reported between-subject effects of early waking on the CARi in 102 community dwelling subjects, when 'early' was defined through cluster analysis as earlier than 0803h (early mean waking time 0649h  $\pm$  0.06; late mean 0943h  $\pm$  0.09).

In contrast, a number of large studies have reported that the CARi is not related to waking time (Pruessner et al., 1997; Kunz-Ebrecht et al., 2004a). For example, Wust et al. (2000) found no association between waking times and the awakening response in over 500 adults, with a wide range of waking times (0420 h-1245). In the current study, time of waking was not correlated with the CARi or AUCg within any shift condition. One explanation for the shift effects in the absence of a linear association between waking time and the CARi might be that there is a threshold time, or a stage of sleep, before which the HPA axis is hypersensitive to awakening. Two studies argue against a purely physiological time threshold. Hucklebridge et al. (2000) found a smaller CARAUC when 11 volunteers were woken at 0400h than 0800h. Born et al. (1999) reported no difference in blood cortisol in 15 volunteers sleeping in a laboratory woken at 0600h or 0900h. Neither of these studies was conducted under typical work conditions, so results may generalise to normal life. Born et al., importantly showed that anticipation of the earlier waking time was associated with an ACTH surge before waking, proving that anticipation pervades sleep. On an early shift pilots typically started work within 90 minutes of waking. Early shifts could be associated with greater prior evening anticipation of stress than for late shifts. It might be that HPA axis reactivity to this anticipated stress is greater during the circadian low. Lower basal levels of cortisol are associated with heightened cortisol reactivity to standardised laboratory stressors (Kudielka et al., 2004). Cortisol reaches its nadir in the early hours of the morning (Spath-Schwalbe et al., 1991) so waking from these low levels might be associated with a hyper-reactivity to anticipated psychological stress. Future research could incorporate alternative methods such as the day reconstruction method for assessing psychological states before and during different work shifts, in association with cortisol monitoring over more than two consecutive days, to further investigate psychobiological interactions (Kahneman et al., 2004).

There were no significant associations between positive affect and cortisol in repeated measures analyses; only an inverse correlation between trait positive affect and the CAR neared significance. This trend is consistent with a study of 70 young men in which EMA happiness predicted a low awakening response (Steptoe et al., 2007a). Several studies based on the Whitehall II cohort found that EMA ratings of happiness predicted lower mean cortisol over the day, after adjusting for covariates including negative affect, but each of these studies included over 200 participants (Steptoe and Wardle, 2005; Steptoe et al., 2005; Steptoe et al.,

2008a). With only 27 participants, it may be that the current study was under-powered to detect associations between cortisol and experienced positive affect. However, as outlined in section 2.2.3, the evidence for associations between positive affect and cortisol in monitoring studies has been mixed. For example, Polk et al. (2005) found that trait negative affect, but not state positive affect, was associated with the CARi in a study of 334 healthy adults. Jacobs et al. (2007) found no association between state or trait positive affect and cortisol in 556 young women studied over 5 days.

I had hypothesised that associations between job strain and cortisol would be mediated by positive affect but the hypothesis was not supported. Table 6.3 and Figure 6.5 show that job strain was weakly correlated with lower positive affect on all three shift conditions, but associations with overall positive affect were not statistically significant ( $r = -0.200$ ,  $p = 0.317$ ). In Chapter 5, job strain had a stronger inverse association with a more evaluative questionnaire measure of positive affect, based on a retrospective assessment of positive affect over the past two weeks ( $r < -0.400$ ,  $p < 0.001$ ). EMA measures of affect are thought to be less prone to recall bias and salience memory heuristics than retrospective measures of affect, so the weaker correlation described in this study may be more representative of true associations between job strain and experienced affect (Csikszentmihalyi and Larson, 1987).

This study was limited by a small and relatively homogenous sample. Measurement of positive affect was limited to how 'happy' respondents had felt in the last 30 minutes. Happiness ratings had a relatively narrow range (0.7-2.6 out of maximum of 4 and mean  $1.9 \pm 0.5$ ), indicating limited variability. Job strain also had a narrow range (0.8 – 2.1, mean  $1.3 \pm 0.4$ ). A scale including a wider range of positive emotions (such as cheerful, lively, at ease, used in the PES scale in Chapter 3) may have been more sensitive to changes in positive affect over the day but would have been more of a burden for participants. It may be that in a larger more representative population sample, with more variability in experienced affect and job strain, the trend between job strain and low EMA positive affect observed in this study might be significant. Positive affect does not appear to be an important mediator of the association between job strain and cortisol. Job strain had a strong independent association with evening cortisol and the diurnal slope in this study, largely independent of positive affect.

Strengths of this study included the detailed sampling protocol from waking to bedtime, over three different shift conditions over six days. This enabled analyses of work shift condition effects, in addition to testing the reliability of associations between job strain and affect with cortisol indicators. Data from only three subjects was excluded owing to sampling delays or missing samples. Adherence to the protocol by pilots was high compared with other salivary cortisol studies in shift workers. Federenko et al. (2004) reported that 9 out of 24 nurses provided complete data and Williams et al. (2005) obtained complete data from 22 out of 32 London underground workers. Weaknesses include a relatively small sample size for between-group comparisons. This meant that effects of potential confounders were adjusted for in a series of separate models, rather than in one combined model. Findings based on this convenience sample of male pilots may not generalise to women or other professions. Ratings of sleep quality and duration were limited to subjective records, which may not accurately reflect objective measures (Jackowska et al., 2011). Similarly self-reported waking time and sampling times were used but previous studies have found good agreement between objective and self-reported waking (Dockray et al., 2008).

In conclusion, this study found that in a sample of healthy male airline pilots, job strain was associated with high evening cortisol and a flatter diurnal decline, independent of type of work shift and positive affect during the day. Further longitudinal research would be required to show whether there is a causal association between job strain and abnormal diurnal cortisol rhythms, and if so, whether these changes could be reversed.

## **Chapter 7 Can well-being be enhanced deliberately to reduce job strain and heart disease risks?**

A critical question from a public health perspective is whether improving well-being offers any potential therapeutic value for the prevention or treatment of heart disease. In previous chapters I have discussed the results of observational studies and laboratory experiments. This evidence supports associations between well-being, work stress and biological outcomes but does not prove the direction of causality. In section 7.1, I introduce the hypothesis that increasing employees' subjective well-being may protect against job strain and the associated physiological consequences. In section 7.2, I discuss whether it is possible to make lasting improvements to well-being. I then review intervention studies from the fields of positive psychology (7.3) and occupational stress management (7.4) which have targeted well-being, highlighting studies which examined biological outcomes. In section 7.5, I focus on mindfulness meditation as a promising intervention to test my hypothesis and discuss the limitations of research to date.

### **7.1 An emerging hypothesis**

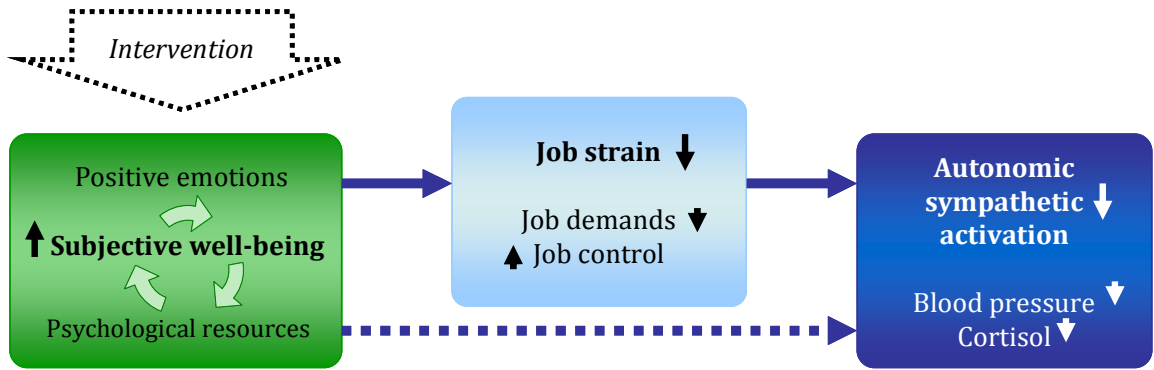
Subjective well-being is associated with a reduced risk of heart disease. The regulation of cardiovascular and neuroendocrine pathways has been implicated in this association. In Chapter 3, I found that positive emotional style was associated with lower perceived stress, lower cortisol response and more rapid blood pressure recovery to an acutely stressful task. Chapter 4 reviewed evidence linking job strain to blood pressure cortisol dysregulation and outlined potential alternative roles for chronic work stress in the association between well-being and heart disease. Chapter 5 suggested that low positive affect could mediate the association between job strain and fatigue. Chapter 6 found that job strain, but not positive affect, was associated with raised evening cortisol.

Building on the evidence presented so far, I hypothesise that in a stressful work environment, increasing workers' subjective well-being will result in lower perceptions of job strain and, over time, lower levels of blood pressure and cortisol (Figure 7.1). Effects on



biological outcomes may be directly associated with an increase in positive emotions or indirectly associated, via decreased job strain.

**Figure 7.1 Hypothesis for the effects of increased well-being in healthy employees**



As discussed in Chapter 1, experiencing positive emotions is one dimension of subjective well-being. According to the broaden-and-build theory, momentary positive emotions broaden people’s mindsets and behavioural repertoires, triggering cycles of positive experiences which build psychological and social resources (Fredrickson, 2001). Mastery, autonomy and relatedness have been identified as core resources for psychological well-being (Ryan and Deci, 2000). In the context of a work environment characterised by high demands and low control, increased subjective well-being could promote a re-appraisal of demands as more achievable challenges. Workers might either *perceive* higher autonomy or take pro-active (problem-focused coping) actions which increase their control over work tasks (Folkman, 2008). The resulting reduction in job strain could lead to a decrease in chronic sympathetic autonomic and neuroendocrine activation (Chandola et al., 2008). An increased frequency of positive emotions may also have a direct influence on the biological stress cascade, by promoting rapid recovery from negative emotions.

This hypothesis specifically applies to healthy working populations. The review in section 1.4 suggested that positive emotions had weaker effects on cardiovascular outcomes in clinical populations, which may reflect more limited influence on advanced disease processes (Chida and Steptoe, 2008). In the longer term, I hypothesise that if higher levels of

subjective well-being could be maintained over many years, lower levels of job strain would be sustained and workers would be at a reduced risk of developing cardiovascular disease relative to workers who sustained a higher level of job strain.

### *Testing the hypothesis*

As discussed in Chapter 4, few studies have investigated whether baseline levels of well-being predict subsequent job strain. Studies which have examined a longitudinal association between positive affect and job strain (Armon et al., 2012) or job satisfaction (Bowling et al., 2010) observed a predictive effect of trait positive affect, rather than attempting to manipulate well-being. I was unable to identify any studies which explicitly tested the hypothesis illustrated in Figure 7.1, so the remainder of this chapter reviews studies which have tested parts of the hypothesis. I aimed to identify an intervention which would drive increases in positive emotions and subjective well-being without changing the work environment.

In this chapter I do not address psychological or pharmacological interventions designed to target mental disorders such as depression or anxiety. For example, cognitive behavioural therapy (CBT) is a recommended treatment for depression (NICE, 2009). CBT aims to change cycles of negative thinking which may be expected to lead to improved well-being indirectly, via a reduction in negative affect. To test my hypothesis I wanted to use an intervention which would directly and primarily result in a sustainable increase in positive affect.

## **7.2 Hedonic adaptation: are lasting changes to well-being possible?**

As discussed in Chapter 1 (section 1.3), twin studies have identified a substantial heritable component to hedonic, evaluative and eudemonic aspects of well-being (Weiss et al., 2008; Archontaki et al., 2013). Brickman and Campbell (1971) proposed the hedonic treadmill theory in which they theorised that happiness and unhappiness are short-lived reactions to a change in circumstances. After a period of adaptation, a new routine becomes normalised and people return to a hedonic set point, or set range (Frederick and Loewenstein 1999). In a widely cited study, Brickman and colleagues (1978) reported that several years after the event, lottery winners were not happier than non-winners and that people with

paraplegia were not substantially less happy than people who can walk. Richards and Huppert (2011) used data from the 1946 birth cohort to demonstrate the stability of well-being. Teacher ratings of positive temperament at age 13 were associated with midlife well-being, independent of sociodemographic variables, childhood cognition and extraversion.

Despite some support for trait-like aspects of well-being, the review in section 1.3 also included evidence that life events can have long-term consequences on well-being (Diener et al., 2006). A longitudinal study by Gardner and Oswald (2007) directly contradicted the small cross-sectional study by Brickman and colleagues; medium-sized lottery winners (£1,000-£120,000) reported small but significant gains in mental well-being two years later, compared with non-winners. Lucas et al. (2003) used data from 24,000 German adults in a 15-year longitudinal study to show that although mean life satisfaction remained relatively constant, marital transitions could be associated with both lasting improvements and decrements. A follow-up study found that one in four of respondents reported a significant change in life satisfaction from the first five years to the last five years of the study (Fujita and Diener, 2005). A meta-analysis of longitudinal studies found that life events influenced affective and evaluative components of well-being differently, with larger and more persistent effects seen for life satisfaction (Luhman 2012).

As discussed in section 1.3i), twin studies have been used to estimate that between a third and a half of the variance in subjective well-being is accounted for by genetic characteristics. Less than 10% of the variance in well-being is typically explained by socioeconomic characteristics (Diener and Lucas, 1999), leading to the theory that the remaining approximately 40% is determined by voluntary cognitive and behavioural actions, or 'what people do' (Lyubomirsky et al., 2005b). In their model of sustainable happiness, Sheldon and Lyubomirsky (2006) proposed that people can sustainably increase their subjective well-being through changes in intentional activity. However, research into affective forecasting suggests that most people are poor at predicting what actions will make them happy in the future (Kahneman et al., 1999; Lee et al., 2012). Cognitive inaccuracies include a tendency to overestimate the intensity and durability of the impact of future events (impact bias). For example, anticipated happiness at getting a higher salary may lead to working long hours rather than spending time with friends or family (Kang et al., 2013). Social relationships

are a stronger predictor of well-being than income, as discussed in section 1.3. There may therefore be justification for interventions to promote actions or cognitions that will effectively enhance well-being.

### **7.3 Interventions to enhance well-being**

#### *Development of positive psychology interventions*

The first published interventions which aimed to enable people to deliberately enhance their happiness were developed by Fordyce in the 1970s, based on characteristics of typically happy people (Fordyce, 1977; 1983). In a series of studies, student participants attended an 8-10 week programme in which they were encouraged to practice up to 14 'fundamentals' of happiness, including: being more active, spending more time socialising, being productive at meaningful work, lowering expectations and prioritising personal happiness. Compared with inactive controls, participants reported significant gains in positive mood and well-being measures three weeks after the program, regardless of how many 'fundamentals' they completed. The majority of students who responded to a questionnaire 9-18 months later (69%) indicated stable or improved happiness.

A growing interest in positive psychology in the late 1990s led to a renewed interest in Fordyce's work and other methods for promoting optimal mental health (Seligman and Csikszentmihalyi, 2000). Fava and colleagues proposed that tasks to build psychological well-being could be integrated into individual or group therapy for patients with affective disorders to help prevent relapse (Fava et al., 1998; Fava and Tomba, 2009). Well-being therapy (WBT) was based on increasing the six aspects of psychological well-being identified by Ryff and Singer (1996), such as mastery, personal growth and autonomy. Seligman later used the phrase 'positive psychotherapy' to describe the use of positive psychology for the treatment of depression (Seligman et al., 2005). Positive psychotherapy (PPT) is defined as a therapeutic approach which aims to build positive emotions, character strengths and meaning to counteract negative symptoms (Seligman et al., 2006). Many of the same exercises described as positive psychotherapy have been used outside therapeutic settings with healthy subjects so I refer to 'positive psychology interventions' (PPIs) to incorporate treatment or

intentional activities that aim to cultivate positive feelings, behaviours or cognitions (Sin and Lyubomirsky, 2009).

### **7.3.1 Types of Positive Psychology Intervention (PPI)**

Table 7.1 lists some examples of PPIs classified as either predominantly cognitive or combining cognitive and behavioural components. Cognitive interventions share the aim of promoting a habitual focus on, and appreciation of, positive aspects of life. One of the simplest interventions, 'three good things', involves participants recording three aspects of their lives they are grateful for each day, which has been found to improve ratings of subjective well-being for up to six months (Seligman et al., 2005). This intervention promotes an immediate positive emotional experience (hedonic well-being) by re-living and savouring positive events but also promotes gratitude, which has been linked to life satisfaction and effective coping (Wood et al., 2010).

Writing exercises may be used to promote evaluative well-being by encouraging positive re-appraisal, a deliberate cognitive process which involves changing one's interpretation of a stressful event to minimise the importance of negative aspects and to identify a positive outcome (Carver and Scheier, 1994). Pennebaker and colleagues also suggested that inhibition of thoughts, feelings and behaviours can act as a physiological stressor, so that writing expressively about distressing experiences can have direct health benefits (Pennebaker and Beall 1986; Pennebaker and Susman 1988; Esterling et al. 1999). King (2001) adapted Pennebaker's written emotional disclosure paradigm and randomised 81 undergraduates to write for 20 minutes each day for four consecutive days about either: visualising their best possible future selves, a traumatic event, both topics, or a non-emotional control topic. Writing about one's best possible self was associated with immediate improvements in mood, and all three emotional writing tasks were associated with improved well-being and fewer self-reported visits to a health centre after five months. Benefits from expressive writing are also hypothesised to arise from an improved sense of emotional self-regulation (Frattaroli, 2006).

**Table 7.1 Examples of positive psychology interventions which focus on cognitive or cognitive and behavioural methods**

<b>Cognitively focused exercises</b>		
PPI	Task	Example
Gratitude journal /'counting your blessings'/three good things	<i>There are many things in our lives, both large and small, that we might be grateful about. Think back over the past week and write down on the lines below up to five things in your life that you are grateful or thankful for.</i>	Undergraduates or adults with a neuromuscular condition counted their blessings weekly or daily in a series of studies. Compared with writing about daily hassles, gratitude predicted increased subjective well-being and positive affect (daily blessings) but had no effect on physical health (Emmons and McCullough, 2003).
Positive writing	<i>Think about your life in the future. Imagine that everything has gone as well as it possibly could. You have worked hard and succeeded at accomplishing all of your life goals. Now, write about what you imagined.</i>	Undergraduates writing for 20 min 3 times per week for three weeks reported feeling less upset, more happy, and getting sick less often than when writing about 3 alternative conditions after 5 months (n=81) (King, 2001).
Positive reappraisal	<i>Think about one negative or stressful thing that happened to you. Practice viewing the situation positively. Is there a 'silver lining'? Practice noticing your thoughts without reacting right away.</i>	Incorporated as one skill within 10 week positive affect intervention for HIV patients. In a pilot study with 11 patients, led to improvements in positive affect (Moskowitz et al., 2012).
Noticing/ capitalising on positive events	<i>Identify a positive event that happened last week. Think back, stop and savour it, write about it, talk about it or post on Facebook.</i>	Dispositional use of capitalising strategies to communicate and celebrate positive events was associated with life satisfaction in undergraduate students (Quoidbach et al., 2010) also included in (Moskowitz et al., 2012).
<b>Behavioural exercises</b>		
PPI	Task	Examples
Acts of kindness	<i>Perform 3 acts of kindness (for anyone you wish) per week and write them down, e.g. "gave my mum a hug when she was stressed by her job", "gave someone some of my lunch", "vacuumed the floor."</i>	9 to 11 year-olds instructed to perform 3 acts of kindness per week over 4 weeks improved subjective well-being and peer acceptance more than students who visited 3 new places (n=415) (Layous et al., 2012).
Identifying signature strengths and using them in new ways	<i>Take the inventory of character strengths assessment (<a href="http://www.authentichappiness.org">www.authentichappiness.org</a>) and use the top 5 strengths in a new and different way each day for 1 week.</i>	Exercise delivered online to users of the Authentic Happiness Website. Recipients reported increased happiness and reduced depressive symptoms for six months versus placebo control (n=136) (Seligman et al., 2005)
Writing and delivering a gratitude letter	<i>You have 1 week to write and deliver a letter of gratitude in person to someone who has been especially kind to you but whom you have never properly thanked.</i>	Exercise delivered online to users of the Authentic Happiness Website. Recipients reported large immediate increases happiness and reduced depressive symptoms maintained for one month versus placebo control (n=150)(Seligman et al., 2005)

Eudemonic well-being could be enhanced by interventions which promote a sense of purpose, autonomy or social relatedness such as those interventions which set achievable behavioural goals. Layous et al. (2012) randomised over 400 school children aged 9 to 11 years to either perform small acts of kindness or to keep track of places they visited for four weeks. Both interventions improved levels of positive affect but pupils were more likely to choose classmates who had conducted the kindness intervention as people they would like to spend time with, indicating that deliberate kindness may promote social acceptance. Seligman and colleagues randomised internet users to either a gratitude visit, recording 'three good things in life' daily, or 'using signature strengths in a new way' in which participants identified their greatest character strengths from an inventory of 24 strengths (such as creativity, love, fairness, forgiveness) and practiced using these strengths in a different way each day (Seligman et al., 2005). The signature strengths intervention was associated with increased happiness and decreased depressive symptoms for six months. The instructions lasted for only a week but participants who continued to benefit at six months were those who spontaneously continued to practice. Identifying and practicing signature strengths is thought to enable individuals to increase the time they spend pursuing engaging activities at which they excel, promoting self-esteem, mastery and intrinsic motivation (Ryan and Deci, 2000; Peterson and Seligman, 2004).

These PPIs and related exercises are often combined into structured programmes of positive psychotherapy. For example, Seligman and colleagues (2006) described a six week group programme for students with mild to moderate depression which was associated with improved satisfaction with life and reduced depressive symptoms at one year follow-up (n=14), compared with a no-treatment control. A 12-week programme resulted in similarly positive outcomes in 11 patients with severe depression, compared with a treatment as usual psychotherapy, with or without antidepressant medication (Seligman et al. 2006).

Table 7.1 does not include mindfulness-based interventions, which are sometimes classified as PPIs (Lyubomirsky and Sin, 2009). Mindfulness-based therapies use meditative attention and concentration practices to improve awareness and emotional regulation. Mindfulness meditation is associated with improvements to subjective well-being, but

traditionally, enhancing positive emotions has not been the primary aim (Sedlmeier et al., 2012). I discuss mindfulness interventions in section 7.5.

### **7.3.2 Effectiveness of PPIs for improving well-being**

Lyubomirsky and Sin (2009) conducted a meta-analysis of 49 PPI trials published between 1977 and 2008, totalling 4,235 participants (median  $n=64$  per study). They reported positive effects on well-being with a moderate mean effect size ( $r=0.29$ , standardised mean difference Cohen's  $d=0.61$ ), with 96% of effect sizes in positive direction. PPIs tended to be more effective for depressed individuals, which could reflect ceiling effects within healthy populations. Multi-component PPI interventions, which involved a variety of skills, were more effective than those that focused on a single skill, consistent with the idea individuals adopt skills that they are interested in, attracted to, and willing to spend time practicing (Schueller and Parks, 2012). Participants recruited into programmes explicitly aiming to increase happiness tended to report greater gains than those unaware of the purpose, raising the possibility that self-fulfilling prophecy effects, or positive response biases, accounted for the effects (Kunda 1990). Lyubomirsky et al. (2011) showed that undergraduates motivated to increase their happiness were those most likely to practice exercises, but that regardless of self-selection effects, only specific (non-control) PPI activities led to improved well-being.

The meta-analysis by Sin and Lyubomirsky (2009) had some important limitations: there was no assessment of study quality, rates of attrition were not reported, quasi-experimental studies based on self-selection were included and mindfulness-based therapies (which do not explicitly seek to promote positive feelings) were included. A more recent meta-analysis of positive interventions by Bolger et al. (2013) included only randomised controlled trials which had been explicitly developed in line with the tradition of positive psychology, i.e. excluding mindfulness-based therapies. This meta-analysis included 39 studies, totalling 6,139 participants. Effect sizes were calculated for subjective well-being (evaluative and hedonic measures), psychological well-being (eudemonic constructs) and depressive symptoms. Effect sizes were in the small to moderate range, markedly lower than reported by Sin and Lyubomirsky (Cohen's  $d$ : 0.34 subjective well-being, 0.20 psychological well-being, 0.23 depressive symptoms, all  $p<0.01$ ). Both meta-analyses found larger effect sizes for longer duration studies, for individual face-to-face therapies compared with group or



self-administered interventions and for referred populations with psychological problems. The authors commented on a lack of studies of high methodological quality. For example, only a minority of studies reported outcomes after 3 or 6 months follow-up. Most studies reported results based on completers only, as opposed to intention-to-treat, which could significantly bias results (Cuijpers et al., 2010). This is particularly important for internet interventions where rates of attrition of 50% or more have been reported (Schueller and Parks, 2012).

### *Effectiveness of PPIs in the workplace*

The systematic reviews described above included only two studies within working populations which were completed outside a university setting. Abbott et al. (2009) randomised 53 sales managers from an Australian industrial organisation to complete a 10-week online resilience training programme or a wait-list group. The content was largely video-based and included training on practicing optimistic thinking, empathy and enhancing positive aspects of life. After 10 weeks, only 7/26 (27%) of the intervention group had completed the programme and 12/26 (46%) responded to follow-up surveys. Respondents gave positive qualitative feedback on the usefulness of the content but cited a lack of time for using the programme. Based on an intention-to-treat analysis, there were no significant intervention effects on happiness, depression, stress or quality of life. Page and Vella-Brodrick (2012) randomised 50 government employees into a group-based 'Working for Wellness' programme or a wait-list control group. Intervention participants attended a class for one hour per week for six weeks which focused on how to identify and apply personal strengths. Of the 31 participants randomised to the intervention, n=29 completed the program, but only n=23 (74%) completed post-intervention survey and n=13 (42%) completed a 6-month follow-up. The intervention was associated with significant improvements in hedonic and eudemonic well-being (Ryff's PWB scale) at six months, based on complete cases.

In order to identify further examples of PPIs in the workplace, I conducted a search within the PsychInfo database. A keyword search for positive psychology interventions generated 579 articles<sup>13</sup>, but limiting results to studies with workplace or job stress as

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<sup>13</sup> Search for keywords "positive psychology" AND (intervention OR trial OR therapy), retrieved 579 articles, 14<sup>th</sup> June 2013

keywords retrieved only 21 articles<sup>14</sup>. The search generated only one controlled trial in a working population which aimed to improve positive psychological outcomes. Luthans et al. (2008) described a web-based intervention which increased 'PsyCap', a measure of psychological capital combining hope, self-efficacy, optimism and resilience. The intervention consisted of just two 1-hour narrated PowerPoint videos over one week which explained resilient thinking and behaviours, including how to set realistic, challenging and valuable goals. The sample size was large, including 186 adults versus a control group, but follow-up was assessed only three days after the second video and attrition was not reported. Elston and Boniwell (2011) described a qualitative study in which six women were coached to use signature strengths at work, resulting in gains in eudemonic and hedonic well-being. Several of the remaining articles retrieved in the search were reviews describing the similarities between coaching (to enhance goal attainment) and positive psychology (to enhance well-being). These articles recommended the use of evidence-based PPIs within the emerging field of coaching psychology, but did not describe any randomised controlled trials using this technique (Britton, 2008; Biswas-Diener, 2009; Grant and Spence, 2010).

I broadened my search strategy to include workplace interventions not explicitly classified as positive psychology interventions by adding the keywords 'positive affect' or 'well-being', which generated 268 articles<sup>15</sup>. Two trials with contrasting findings applied the written emotional disclosure paradigm. Kirk et al. (2011) reported increased positive affect in 46 employed adults two weeks after three days of writing about their emotions during a work day, compared with those who described the events of a non-work day. Ashley et al. (2013) found no intervention effects on psychological health in 77 teachers following completion of emotional disclosure writing tasks, compared with a control writing task.

The literature search did not identify further PPI trials but more than 20 articles described stress management interventions, which are described in section 7.4. Five articles described trials using mindfulness-based stress reduction, which are discussed in section 7.5.

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<sup>14</sup> Search for keywords "positive psychology" AND (intervention OR trial) AND (workplace OR "work stress" OR "occupational stress" OR "job stress" OR "job strain"), retrieved 21 articles, 14<sup>th</sup> June 2013

<sup>15</sup> Search for keywords ("positive psychology" OR well-being OR "positive affect") AND (intervention OR trial) AND (workplace OR "work stress" OR "occupational stress" OR "job stress" OR "job strain"), retrieved 268 articles, 14<sup>th</sup> June 2013

### 7.3.3 Influence of PPIs on biological processes relevant to CVD

Evidence for physiological effects of PPIs is lacking. One paper reported a reduction in cholesterol after two 5-week trials of affectionate writing, compared with a control writing condition, but psychological effects were not reported (Ffloyd et al. 2007). Several early emotional expression experiments reported benefits to immune function (Pennebaker et al. 1988; Esterling et al. 1994), but a systematic review of emotional disclosure studies did not find evidence for objective physical health benefits (Meads and Nouwen 2005). A more recent study found no main effects of a written emotional disclosure intervention on cardiovascular reactivity to stress in healthy young adults (O'Connor and Ashley, 2008).

Several recent trials have reported the use of PPI techniques as an adjunct to behaviour change programmes. Peterson et al. (2012) randomised 242 patients after percutaneous coronary intervention to either an education-based physical activity programme or the same programme with the addition of bimonthly phone calls to induce positive affect, such as by reminding patients to savour positive thoughts. Positive affect group participants also received small unexpected gifts in the post, such as a t-shirt or magazine. After 12 months, the positive affect group were 1.7 times more likely to reach their exercise goal. However, a similar intervention in asthma patients showed no effect on physical activity (Mancuso et al., 2012). Ogedegbe et al. (2012) tested a positive affect and self affirmation intervention to improve medication adherence in older patients with hypertension. There was a borderline effect on rates of adherence (42% intervention group vs. 36% control group,  $p=0.049$ ) but no significant difference in blood pressure reduction. These studies indicate that positive psychology might help to promote healthy behaviours but no evidence of direct 'mind-body' biological effects. A phone-based intervention for patients hospitalised with acute cardiac disease involved eight weekly PPI exercises based on optimism, kindness and gratitude (Huffman et al., 2011). Nine out of ten patients completed follow-up measures. There was a trend for reduced anxiety and depression compared with relaxation and inactive comparison groups, but biological outcomes were not reported.

#### *Suitability of PPIs for testing the hypothesis in Figure 7.1*

The evidence above suggests that the practice of specific positive behaviours and cognitive techniques can lead to gains in subjective well-being for up to one year, at least for motivated

participants. The popularity of multi-component approaches, whilst offering choice to participants, makes it difficult to identify whether any specific skills are more effective for promoting well-being. Much of the existing evidence for PPIs is based on small-scale trials, convenience samples of students or self-selected volunteers recruited via the internet. The few PPI-based interventions in working populations have reported high levels of attrition, which may suggest a lack of engagement or perceived lack of relevance in a busy workplace setting. Online administration of PPIs offers potential advantages in terms of standardisation of delivery, low cost, user convenience and scalability, but the quality of evaluation of such interventions to date has been low. Most studies report subjective well-being outcomes within adherent populations after a limited follow-up period, which may over-estimate effectiveness. It is unclear whether the PPIs described above influence biological processes.

## **7.4 Workplace stress management approaches**

A stress management intervention (SMI) has been defined as any activity or program initiated by an organisation that focuses on reducing the presence of work-related stressors or on assisting individuals to minimise the negative outcomes of exposure to these stressors (Ivancevich et al., 1990). Most SMIs seek to improve well-being as an indirect consequence of tackling the negative emotions, cognitions and behaviours associated with stress at work, but in this section I highlight some relevant exceptions.

### **7.4.1 Types of Stress Management Intervention (SMI)**

Interventions can be broadly classified as organisation-focused, person-focused, or both (Semmer, 2010). It has been argued that the prevention and management of workplace stress requires organisation level interventions, because it is the organisation that creates the stress (Michie, 2002). However, organisation level interventions are unlikely to be suitable to test the hypothesis that positive affect directly influences work stress, since these interventions tend to alter exposure to work tasks (e.g. to provide greater control), conditions (e.g. reduced workload) or social support (e.g. providing supervisor training) (Semmer, 2010). A recent exception was an American study which evaluated the effects of a School-Wide Positive Behavioural Intervention (SWPBIS) on teacher burnout and self-efficacy across 40 elementary schools (Ross et al., 2012). The SWPBIS programme aimed to create a positive and supportive

culture in schools by creating opportunities for positive interactions between teachers and students and by rewarding students' pro-social behaviour. In schools which had implemented SWPBIS with high fidelity, teachers reported lower burnout. This suggests that promoting a positive environment may help to reduce perceptions of work stress but the SWPBIS is a complex intervention which could not easily be applied outside the elementary school setting.

Person-focused interventions, also referred to as Stress Management Training, typically involve attending a series of weekly group sessions which teach a combination of cognitive-behavioural skills training (CBST) and physical relaxation techniques. CBST is based on the same principles as cognitive-behavioural therapy and involves identifying stress triggers, identifying maladaptive patterns of interpretation and coping, then modifying cognitive and behavioural responses using problem-solving or role play (Giardini Murta et al., 2007). CBST may also target specific competences associated with active coping such as assertiveness, conflict resolution, time-management or anger management (Semmer, 2010). Relaxation approaches include Progressive Muscle Relaxation and biofeedback, in which participants deliberately relax specific muscles (Murphy, 1996). Several recent reviews of SMIs include meditation as a relaxation approach (Richardson and Rothstein, 2008; Semmer, 2010; Bhui et al., 2012). In this chapter I classify mindfulness-based stress reduction as a separate category of intervention, since any physical effects are secondary to emotional regulation (Holzel, 2011).

A meta-analysis published in 2008 reviewed 55 SMIs and reported a significant medium to large effect ( $d=0.53$ ) on various psychological stress outcomes (Richardson and Rothstein, 2008). CBST approaches were associated with larger, more consistent effects than relaxation-focused or combined approaches, but there was considerable heterogeneity between studies.

#### **7.4.2 Effectiveness of workplace SMIs for enhancing well-being**

In the Richardson and Rothstein meta-analysis only two small studies specifically measured subjective well-being outcomes. A small 3-day emotional writing study by Alford et al. (2005) increased positive affect after one week. A taught relaxation technique to introduce daily 15-minute relaxation breaks had no effect on happiness (Peters et al., 1977). In recent years, the

design of SMT programmes does appear to have been influenced by positive psychology and several trials retrieved in the literature search have emphasised the development of positive psychological resources to combat work stress. Burton et al. (2009) described the rationale for a 13-week workplace resilience programme targeting positive emotions, cognitive flexibility, life meaning, social support and physical activity as an active coping strategy. This 'READY' programme was associated with reduced stress and total cholesterol and gains mastery, autonomy and positive emotions in a pilot study with 16 employees (Burton et al., 2010). Hahn et al. (2011) taught 48 employees a recovery training programme over nine hours which targeted psychological detachment, relaxation, mastery experiences and control during off-job time. The programme was associated with improvements in mastery and control after one week and improved self-efficacy and reduced perceived stress after three weeks compared with an inactive control group. Rose et al. (2013) described a self-guided six session multi-media work stress management programme combining elements from CBST, relaxation and PPIs (SMART-OP) which reduced perceived stress compared with an attention control group, based on an uncontrolled pilot study involving 59 healthy graduate students.

#### **7.4.3 Influence of stress management interventions on biological processes**

There is some evidence that relaxation-focused and combination SMIs can directly influence physiological processes in stressed workers, at least in the short-term (Murphy, 1996; van der Klink et al., 2001). Deliberate relaxation is thought to temporarily alter autonomic balance and activate the parasympathetic nervous system (Jacobs, 2001). The meta-analysis by Richardson and Rothstein (2008) suggested that multi-component and relaxation-focused interventions may have a small effect on blood pressure, but their review included only seven relevant studies which were all based on small samples ( $n < 60$ ) and short-term follow-up.

Lucini et al. (2007) reported a significant reduction in low frequency respiratory rate variability and a trend for lower systolic arterial pressure in 91 white collar workers after brief cognitive restructuring and relaxation training versus a sham programme, but effects on job stress were not reported. Limm et al. (2011) described a cognitive-focused training programme for steel workers based on the ERI model, based on a 2-day seminar and two refresher session over six months. Assessment in 154 employees 12 months later revealed that the intervention was associated with a trend for lower ERI and depressive symptoms and

a significant reduction in  $\alpha$ -amylase secretion over the day (as an indicator of sympathetic activity). There was no change in salivary cortisol compared with controls.

Of those interventions explicitly targeting positive psychological resources, the READY pilot programme was associated with a reduction in total cholesterol but also promoted physical activity, which may have direct effects on lipids (Burton et al., 2010; Kelley et al., 2012). SMART-OP was not associated with differences in heart rate variability or blood pressure reactivity to the Trier Social Stress Task relative to control (Rose et al., 2013). McCraty and colleagues (2003) introduced a 16-hour programme for hypertensive employees which combined instruction in positive emotion re-focusing (positive reappraisal) and heart rate variability (HRV) biofeedback. Three months later the treatment group (n=20) exhibited a significant reduction in systolic blood pressure versus the control group (n=20), which was correlated with reduced stress symptoms. A similar trial involving deliberate positive emotion generation and HRV biofeedback in 40 physicians resulted in reduced stress after 28 days but no effect on blood pressure compared with controls (Lemaire et al., 2011).

#### *Suitability of SMIs for testing the hypothesis in Figure 7.1*

Workplace SMIs which explicitly target negative emotions and cognitions are unsuitable for testing the influence of well-being on job strain. Studies which have examined physiological outcomes do offer some support for the second part of the hypothesis (an association between decreased perceptions of job stress and altered autonomic balance), but no trials with biological outcomes have reported an association with job strain based on the Demand-Control model. Relaxation training may promote a direct reduction in sympathetic activation but effects on work stress are less consistent than for cognitive approaches (Richardson and Rothstein, 2008). Workplace trials using biofeedback devices have typically involved small samples, perhaps owing to the cost of mobile digital biofeedback devices which limits their suitability for large-scale public health interventions (Lemaire et al., 2011). As the cost of technology decreases, there may be more scope to incorporate biofeedback into larger trials.

Workplace interventions which primarily target positive psychological resources are a relatively new phenomenon but several small trials have shown promising short-term impacts on well-being. Effects on biological processes are unclear, since combination approaches with physical exercise or relaxation have been used. In general, research into SMIs

has been criticised as a 'black box', with poor explanations of how effects are produced, by which mechanisms, in which context, and for the benefit of whom (Biron, 2012). Positively, the READY and SMART-OP programmes include standardised manuals to enable consistency of delivery and facilitate understanding of the effects (Burton et al., 2009; Rose et al., 2013). As noted in the section on PPIs above (section 7.3), computer-based programmes offer a potentially low cost means to deliver standardised interventions on a large scale and at the user's convenience. To date there is no evidence that online SMIs alter physiological processes (Luthans et al., 2008; Rose et al., 2013).

## **7.5 Mindfulness-based approaches to enhancing well-being**

Literature searches for positive psychology interventions and workplace well-being interventions generated a number of studies which involved mindfulness meditation in the workplace, e.g. Klatt et al. (2009), Wolever et al. (2012). A recent meta-analysis reported that mindfulness-based therapies were moderately effective for improving anxiety and negative mood symptoms in patients with medical conditions across 39 studies (Hofmann et al., 2010). A review of 10 trials in healthy populations also reported a significant effect on stress reduction (Chiesa and Serretti, 2009). A review by Sedlmeier (2012) found that mindfulness meditation was associated with significant improvements in well-being (17 studies) and positive affect (6 studies). This section explains the concept of mindfulness and how mindfulness-based approaches are distinct from other psychological therapies. I outline some evidence for neurobiological mechanisms underlying mindfulness meditation, followed by a more systematic review of the effects of mindfulness meditation in the workplace.

### **7.5.1 Defining mindfulness and mindfulness-based therapies**

Mindfulness can be defined as a mental state characterised by full awareness of one's present moment experience, with an attitude of openness and nonjudgmental acceptance (Brown and Ryan, 2003). Mindfulness can also refer to a general trait-like tendency to be 'mindful' in daily life, in other words, to routinely pay attention to physical, cognitive and emotional experiences without over-reaction or denial. Mindfulness can be developed through the practice of mindfulness meditation, an exercise which involves focusing one's attention and allowing thoughts and emotions to pass through conscious awareness without judgment.



### *Origins of mindfulness meditation to enhance well-being*

The benefits of meditation and mindfulness have been emphasised in Buddhism for over 2,500 years. Buddhist tradition makes a clear distinction between transient affective states that are directly aroused by sensory or internal stimuli, and a deeper intrinsic well-being (*sukha*) which arises naturally from attentional, emotional and cognitive balance of the mind. Buddhist meditative practice does not aim to suppress either destructive (negative) or pleasant mental states, but to identify how they arise, how they are experienced and how they influence oneself and others. Cultivation of mindfulness helps to 'free' the mind of all stimulus-driven states, resulting in a natural and enduring sense of well-being, which is akin to psychological flourishing or eudemonic well-being (Cahn and Polich, 2006; Jung et al., 2012). Mindfulness meditation is based on the tradition of 'Vipassana' or insight meditation and is conceptually distinct from concentrative types of meditation ('Samantha'), such as Zen or Transcendental Meditation (TM). TM involves repetition of a mantra, leading to 'transcendence' from the waking state to a state of deep relaxation. Zen meditation involves focussing on an object of meditation such as one's breath, an idea or image. Only mindfulness meditation emphasises cultivating moment-to-moment awareness of thoughts and emotions (Sedlmeier et al., 2012). Buddhist meditation teachers may combine several different meditative approaches in the pursuit of *sukha*.

### *Adaptation of mindfulness for secular clinical practice*

The first clinical application of mindfulness as a therapeutic strategy has been attributed to Jon Kabat-Zinn (Kabat-Zinn, 1982; Keng et al., 2011). Kabat-Zinn developed Mindfulness-Based Stress Reduction (MBSR) as a standardised secular course of intensive mindfulness meditation training to help chronic disease patients to become more aware and less reactive to physical and psychological states. The aim was to enable patients to recognise and alter habitual maladaptive patterns of thinking and behaviour (Kabat-Zinn, 1990). MBSR consists of an eight week course of two and a half hour group sessions for mindfulness instruction and training, plus daily home practice and a 7-hour retreat. Meditative practices typically include: sitting meditation, maintaining focus on the breath whilst allowing thoughts and emotions to come and go; 'body scan', a movement of attention through the body observing physical sensations; and Hatha yoga, stretches and postures designed to enhance physical awareness and strengthen the musculoskeletal system.

Unlike cognitively-focused approaches to stress reduction such as CBT and CBST, mindfulness meditation does not set out to deliberately change the content or evaluation of negative thoughts or emotions, but rather to change one's awareness of, and relationship to, those cognitions. The effect is to dissociate an individual from potentially maladaptive reactions (Kuyken et al., 2010). Mindfulness-Based Cognitive Therapy (MBCT) combines both mindfulness meditation and cognitive strategies to prevent relapse in remitted depression (Teasdale et al., 2000). MBCT is recommended for the treatment of recurrent depression by the National Institute for Clinical Excellence (NICE, 2009).

*Does mindfulness 'primarily' enhance positive affect, or reduce negative affect?*

A critical question for using mindfulness meditation to test the hypothesis in Figure 7.1 is whether increases in positive affect and well-being can be thought of as a driver of reduced stress, or simply a consequence. According to Buddhist thinking, mindfulness allows one's natural state of well-being to emerge by letting stimulus-driven thoughts and emotions pass, rather than 'creating' well-being. A more modern interpretation suggests that openly experiencing the present moment can effectively counter the effects of stressors, because excessive orientation to the past or future is related to feelings of depression or anxiety (Kabat-Zinn 2003). An alternative argument suggests that since pleasant events and emotions are usually less enduring, intense, and attention-grabbing than unpleasant emotions (Baumeister et al., 2001), they may be more easily overlooked than their unpleasant counterparts. Mindful awareness may therefore help people to pay attention to fleeting pleasant events or emotions and to generate more enjoyment from pleasant activities (Geschwind et al., 2011).

Relatively little research has examined whether mindfulness has distinct or dominant effects on positive or negative emotions. The meta-analysis by Sedlmeier et al. (2012) split out mindfulness studies which specifically looked at positive versus negative emotions and found a very similar effect size for positive ( $\bar{r}=0.26$ , 6 studies) and negative emotions (0.20, 8 studies). A recent trial used experience sampling over 6 days before and after MBCT in patients with recurrent depression (Geschwind et al., 2011). Compared with a wait-list control group, mindfulness therapy increased daily experiences of positive emotions, even after adjusting for reductions in depressive symptoms, negative emotion, rumination, and worry. Participants were more likely to appraise daily-life situations as positive.

Garland et al. (2009) suggested that mindful states facilitate positive reappraisal, a meaning-based coping strategy in which stressful events are re-construed as benign, beneficial and/or meaningful (Folkman, 1997; Garland et al., 2009). The same authors later used path analysis to demonstrate that increased positive reappraisal partially mediated the association between greater mindfulness and lower perceived stress in over 300 participants after an 8-week mindfulness-based stress and pain management (MSPM) course, based on MBSR (Garland et al., 2011). The MSPM programme was not described in detail, but like MBCT may have explicitly discussed coping and cognitive appraisal strategies, making it difficult to assess the unique effects of mindfulness meditation. A recent study suggested that mindfulness leads to a bias for positive emotional processing: 28 students randomised to a 12-week meditation course showed significantly greater recall of positive words, but no difference in negative words, in a memory recall task (Roberts-Wolfe et al., 2012).

Whilst some authors have categorised mindfulness training as a PPI (Sin and Lyubomirsky, 2009), the practice of mindfulness meditation is an exercise in awareness and acceptance of the present moment, not deliberately cultivating positive emotion. In contrast, Loving Kindness Meditation (LKM) and Compassion Meditation (CM) are meditative techniques which involve directing one's emotions toward warm and tender feelings in an open-hearted way (Fredrickson et al., 2008b). LKM and CM offer promise as an interventions for increasing mindfulness and promoting well-being, but empirical research is considerably less established than for mindfulness meditation (Hofmann et al., 2011). In this section I concentrate on MBSR and closely-related interventions in which mindfulness meditation is the core focus.

In summary, positive affect does appear to play a significant role in the effectiveness of mindfulness-based therapies, but it remains unclear to what extent changes in positive emotions are drivers or consequences of reduced negative emotions.

### *Measuring mindfulness*

Several self-report questionnaire measures of dispositional, or trait, mindfulness are widely used. Buchheld et al. (2001) developed the Freiburg Mindfulness Inventory (FMI) by reviewing the literature to identify items relevant to the concept of mindfulness, inviting expert meditators to rate statements for relevance and conducting psychometric analysis and

Principle Component Analysis. This generated a 30-item questionnaire assessing nonjudgmental present-moment observation and openness to negative experience. FMI items include, “I watch my feelings without becoming lost in them,” and “I am open to the experience of the present moment,” rated on a 4-point frequency scale. A 14-item version was subsequently validated in expert and non-meditators, clinical and working populations, and has been shown to be sensitive to change after short-term mindfulness meditation training (Walach et al., 2006; Trousselard et al., 2010).

Alternative measures include the Mindfulness and Attention Awareness Scale (MAAS) (Brown and Ryan, 2003), a 15-item scale which assesses attention and awareness but not nonjudgmental acceptance. The Kentucky Inventory of Mindfulness Scale (KIMS) is a 39-item instrument designed to measure four distinct aspects of mindfulness: observing, describing, acting with awareness and accepting without judgment. The Cognitive and Affective Mindfulness Scale (CAMS) measures the frequency of mindful daily experience (Feldman 2004). The Mindfulness Questionnaire (Chadwick et al 2005) assesses a mindful approach to distressing thoughts and images. Baer et al (2006) showed that all five scales above were positively correlated. They proposed the Five Facet Mindfulness Questionnaire (FFMQ), based on factor analyses of students’ responses to all the combined items of the previous scales. The FFMQ includes the four KIMS factors plus non-reactivity to inner experience.

Questionnaire measures have been criticised for failing to share a common conceptual definition of mindfulness (Grossman, 2008). The extent to which self-reported mindfulness, based on self-belief, reflects how mindful people are in daily life is also debatable. Questionnaire measures of trait mindfulness are reliably correlated with positive psychological attributes including life satisfaction, competence, autonomy and positive affect (Brown and Ryan, 2003) and inversely correlated with depression, rumination and neuroticism (Giluk, 2009; Raes and Williams, 2010). Dispositional mindfulness has also been associated with reduced amygdala activation, part of the limbic circuitry involved in fear conditioning (Way et al., 2010).

### 7.5.2 Mindfulness meditation and mechanisms of action

In addition to reducing symptoms of mental distress and improving well-being, mindfulness-based therapies have been effective for treating chronic pain (Grossman et al., 2007), behavioural disorders including binge eating (Courbasson et al., 2011) and substance abuse (Brewer et al., 2009). Short-term effects on improved attention (Tang et al., 2007; Zeidan et al., 2010) and working memory (Jha et al., 2010) have been reported. A number of studies have found that mindfulness meditation is associated with changes in physical health including improved immune function (Davidson et al., 2003; Lengacher et al., 2011), telomerase activity (Jacobs et al., 2011) and markers of inflammation (Rosenkranz et al., 2013). A recent review of found some support for reductions in blood pressure in normotensive and hypertensive populations (Chiesa and Serretti 2010), but commented that the majority of studies were small-scale, of low quality and without long-term follow-up. Uncontrolled and small trials suggest that meditation may reduce cortisol release (Carlson et al. 2007; Brand et al. 2012) but results have not been consistent (Gex-Fabry et al. 2011).

#### *Potential mechanisms linking mindfulness, emotion and biological processes*

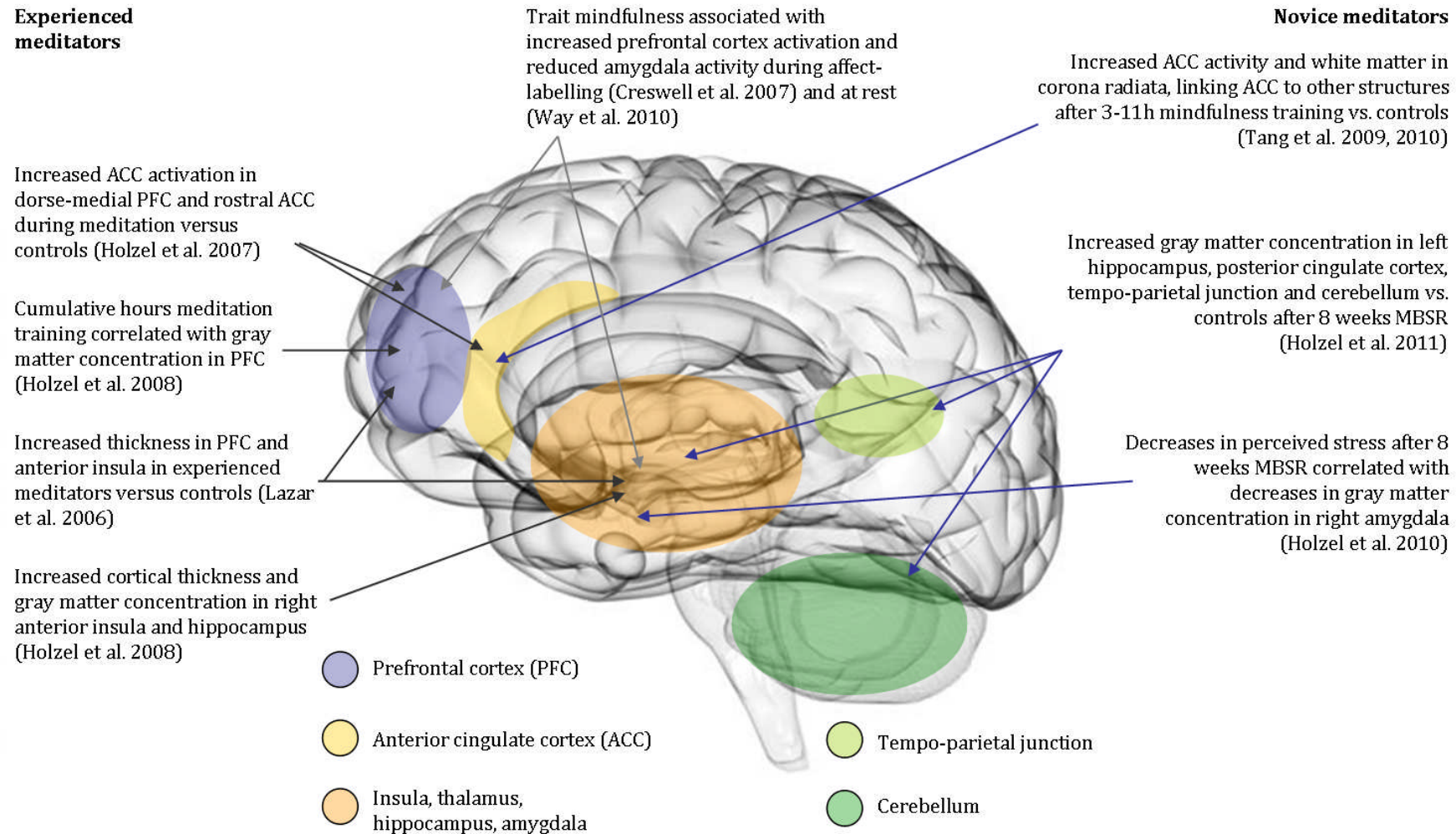
The neurobiological mechanisms underlying the effects of mindfulness meditation have been the subject a considerable body of research. Holzel et al. (2011) proposed that mindfulness exerts its effects through improved self-regulation, a process arising from increased attention regulation, body awareness, emotion regulation and a more detached perspective on the self. Figure 7.2 illustrates areas of the brain implicated in functional MRI studies of meditators experienced in mindfulness (or Vipassana/insight meditation) (black arrows) and novice meditators learning MBSR (blue arrows). Imaging studies have highlighted the limbic system, including the hippocampus, amygdala and cingular cortex. The limbic system is involved in processing emotion and memory and is modulated by cognitive appraisals in the prefrontal cortex (PFC) (Banks et al., 2007). During meditation, activity in the PFC increases and appears to exert an inhibitory top-down influence on the amygdala (Farb et al., 2007). The amygdala generates fear and arousal emotions which can activate the sympathetic nervous system via projections to the hypothalamus. After 8-weeks MBSR, Holzel et al. (2010) found that decreases in perceived stress were associated with reduced grey matter concentration in the amygdala, indicating reduced activity. Increases in activity of the hippocampus and insula

are hypothesised to be associated with less automatic reactivity to emotion and an increased sense of detachment (Farb et al., 2007; Farb et al., 2012).

Mindfulness training is also associated with increased activity in the anterior cingulate cortex (ACC), an area associated with maintenance of attention and regulation of the autonomic nervous system (Tang et al., 2010). Tang et al. (2009) showed that after only five days of mindfulness meditation-based training, activity in the ACC increased versus a relaxation control intervention and was correlated with increased heart rate variability. Ditto et al. (2006) investigated the body scan element of mindfulness meditation which was associated with reduced diastolic blood pressure in women compared with a relaxation control activity. Mindfulness meditation differs from relaxation programmes in which participants are asked to consciously control breathing and muscle tension; mindfulness body scan instructions would be to acknowledge physical tension, but not to consciously alter it.

Although all the studies in section 7.5.2 have explicitly examined the correlates or effects of mindfulness/Vipassana meditation practice, it should be noted that few studies have compared neural correlates or effects of different types of meditation. Neural correlates or effects may not be distinct from TM or other meditative techniques (Cahn and Polich, 2006; Lee et al., 2012).

**Figure 7.2 Overview of brain areas linked to mindfulness meditation**



### **7.5.3 A review of the effects of mindfulness meditation in the workplace**

My previous database searches had not identified any trials testing the effects of mindfulness meditation on job strain. I conducted a systematic review of mindfulness studies conducted in working populations to check for evidence that mindfulness meditation a) improves positive psychological well-being; b) reduces work-related stress; c) influences biological processes, in particular blood pressure and cortisol.

#### *Search strategy*

I searched for mindfulness-based interventions in working populations which had examined well-being or stress outcomes in PubMed and PsycInfo<sup>16</sup>. The literature search resulted in 280 articles in PubMed and an additional 42 articles in PsychInfo. Abstracts were screened and articles fulfilling the following requirements were included: i) empirical mindfulness-based intervention administered in an employment setting and/or to a working population, ii) positive psychological well-being and/or work stress and/or objective biological outcome assessed, iii) non-student population, iv) full text article available, v) peer-reviewed journal article. Studies in students were excluded because their work demands and control over work may not be comparable to paid employees. Fourteen articles fitted the criteria. Details of sample sizes, loss to follow-up, programme content and outcomes (including effect sizes, where reported) were extracted (Table 7.2).

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<sup>16</sup> Search terms: (mindfulness OR mindful) AND ("well-being" OR "positive affect" OR "positive emotion" OR stress OR "job strain") AND (intervention OR trial OR therapy) AND (workplace OR "work setting" OR occupational OR employee), retrieved 322 articles 15<sup>th</sup> June 2013



**Table 7.2 Mindfulness meditation-based interventions in working populations**

Lead author (date)	Baseline sample	ITT vs CC, loss to follow-up	Mindfulness programme	Psychological outcomes	Biological outcomes
Bazarako (2013)	n=41 female nurses employed by private healthcare company. <i>(uncontrolled)</i>	CC analysis. Attrition at 4mth post intervention 12% (n=36)	8-week "tMBSR" programme: 1*day initial retreat, 6*weekly 1.5hr group teleconference mindfulness session, 1*day final retreat. Daily 25-30min practice, workbooks and practice logs (mean involvement 50.3hrs).	Sig. changes over time: PSS, Copenhagen burnout inventory, SF-12 (general health, vitality, social functioning, emotional stability, mental health), serenity, empathy, self-compassion <i>NS: SF-12 physical functioning, bodily pain.</i>	
Malarkey (2013)	n=186 university staff with raised CRP >3.0mg/ml at risk of CVD:n=93 active, n=93 education control. <i>Exclusion: psychiatric disorder, pregnancy, major life stress in past 2 months, excessive smoking, exercise or drinking, cold in past month, BMI &gt;40, previous mind-body practice.</i>	CC analysis. Attrition at 8wk: 12% active, 9.7% control.	MBI-Id: 8*1hr weekly MBSR + 20min/day formal MM practice Programme included reflective writing, group sharing, mindfulness instruction, yoga and meditation. <i>Control group completed a time-matched education programme.</i>	Sig vs control: TMS mindfulness at 8wk and 1 yr. <i>NS vs control: PSS, depression or sleep quality.</i>	<i>No group differences in CRP, IL-6, leptin, salivary cortisol assessed over 3 days at 4 time points. NS trend for lower CRP in MBI group (p=0.08). Larger MBI-Id effect for participants with baseline BMI&lt;30.</i>
Hulsheger (2012)	n=203 employees in interactive service roles recruited with flyers, enrolled by post. Randomised to n=102 active; n=101 WL. <i>(n=50 active &amp; n=51 WL returned surveys. 37 excluded, including n=19 for &lt;6min/day meditation. Final sample n=22 active &amp; n=42 WL).</i>	CC analysis based on n=64. Attrition/exclusion: 78% active, WL 60% control.	Self-guided programme of MBCT and MBSR exercises spanning 10 working days (2 weeks), including Loving Kindness Meditation + 2*daily 3min meditation practice. Written instructions plus guided CD for audio. Daily meditation diary & mindfulness qre.	Sig vs WL control: daily MAAS mindfulness (state), emotional exhaustion (MBI subscale), job satisfaction.	
Wolever (2012)	n=239 insurance employees randomised to: n=96 Mindfulness at Work, M@W (active), n=90 yoga (active comparison), n=53 WL. <i>Inclusion: score &gt;16 PSS, no chronic medical condition, no regular meditation or yoga.</i>	ITT analysis. Attrition at 12wk: 15% M@W, 16% yoga, 11% WL control.	12*1hr weekly Mindfulness at Work groups + 2hr retreat. Stress management based on MM principles explicitly targeting work-related stress, work-life balance.	Sig. vs WL control: PPS*, Pittsburgh Sleep Quality, CAMS-R Mindfulness. <i>(Effect size for M@W intervention only not reported).</i> <i>NS: CES-D, Work Limitations Questionnaire (productivity), no difference yoga vs M@W.</i>	Sig vs WL control: increased heart rhythm coherence ratio of HRV in preparation for a stressful event. <i>NS: breathing rate clinic, blood pressure.</i>

**Table 7.2 Mindfulness meditation-based interventions in working populations (continued)**

Lead author (date)	Baseline sample	ITT vs CC, loss to follow-up	Mindfulness programme	Psychological outcomes	Biological outcomes
Geary & Rosenthal (2011)	n=153 university hospital employees: n=59 academic employees allocated to active; n=94 healthcare workers allocated to WL.	CC analysis. Attrition at 8wk ?. Attrition at 1yr: 8.5% active; 48% WL control.	8*3hr weekly MBSR groups + 8hr retreat.	Sig. vs WL control: PPS, SCL-90 General Symptom Checklist, SF-36 ( <i>except physical measures</i> ) , Daily Spiritual Experience.	<i>NS: 5-min pulse rate variability.</i>
Jha (2010)	n=60 US marines: n=31 pre-deployment marines (active), n=17 pre-deployment controls, n=12 civilian controls <i>Inclusion: no prior mindfulness experience.</i>	CC analysis. At 10 weeks 6.4% (2/31) excluded for failure to adhere to intervention.	8*2hr weekly groups + 8hr retreat + 30min daily homework (& log) + 15-min individual interview. M-Fit mind fitness training developed for predeployment, including didactic teaching on stress resilience.	No significant group effects. Active group divided into high and low practice times. High practice associated with lower PANAS negative affect, higher positive affect. Practice time correlated with PANAS and working memory effects.	High practice associated with improved working memory capacity via operation span task vs low practice and control.
Krasner (2009)	n=70 primary care physicians. <i>(uncontrolled)</i>	ITT analysis based on mixed-effects models across 5 survey points, baseline to 15mths. Attrition 27% at 15mth	8* 2.5hr weekly groups + 7hr retreat + maintenance (10*2.5hr monthly sessions). Sessions included teaching on 8 themes associated with stress at work, mindfulness meditation, narrative writing and group discussion.	Sig. changes over time: 2-Factor Mindfulness, MBI (all 3 scales), empathy, Physician Belief Scale (psychosocial orientation), POMS mood disturbance, stability & conscientiousness. ( <i>Effect sizes at 15mth: mindfulness d=1.12, POMS total d=0.69, POMS vigor 0.42, empathy d=0.45</i> ).	
Klatt (2008)	n=48 university staff randomised to n=24 active; n=24 WL control. <i>Inclusion: BMI&lt;30, &lt;30min exercise daily, no chronic illness, no regular yoga.</i>	CC analysis. Attrition at 6wk: 8.3% active, 17% control.	6*1hr weekly MBSR at lunchtime + 20min daily meditation/yoga with guided CD, 4days/wk, included formal education element and yoga stretches.	Sig. vs WL control: PSS, MAAS Mindfulness, Pittsburgh Sleep Quality Index (specific subscales only). ( <i>Effect sizes within active group mindfulness d=0.56, PSS=0.73, sleep quality d=0.54</i> ).	<i>NS: salivary cortisol (2 consecutive sampling days pre-intervention post-waking, 1pm, 10pm vs 1 day each week vs 1wk post intervention).</i>
Mackenzie (2006)	n=30 nurses and nurse aides randomised to n=16 active; n=14 WL control. 29/30 female.	CC analysis. Attrition at 4wk ?, study includes all with valid pre/post data.	4*30min weekly MBSR groups + manual + 10min guided CD, 5days/wk.	Sig. vs WL control: Relaxation, MBI emotional exhaustion & depersonalisation, Satisfaction with Life ( <i>Large effect sizes <math>\eta^2 &gt; 0.15</math></i> ). <i>NS: Job satisfaction, Optimism.</i>	

**Table 7.2 Mindfulness meditation-based interventions in working populations (continued)**

Lead author (date)	Baseline sample	ITT vs CC, loss to follow-up	Mindfulness programme	Psychological outcomes	Biological outcomes
Schenstrom (2006)	n=52 primary care healthcare personnel. ( <i>uncontrolled</i> )	CC analysis based on n=48 post intervention (8% attrition), n=41 at 3 months (21% attrition).	7-day (50 hour) programme divided into 3*2-day workshops, 1*1-day. Mindfulness-based cognitive attitude training, formal & informal mindfulness practice, cognitive theory. Practice CD provided for home use.	Sig. changes over time: MAAS mindfulness, quality of life, perceived stress (2 visual analogue scales: work and non-work). Results stable at 3mth follow-up. Higher practice time, stronger effects.	
Cohen-Katz (2005)	n=27 nurses randomised to n=14 active; n=13 WL control.	CC analysis. Attrition at 8wk 14%, 3mth post intervention 29%.	8*2.5hr weekly MBSR groups + 6hr retreat + 6days/wk home practice with audiotapes.	Sig vs WL control: MBI emotional exhaustion & personal accomplishment, MAAS mindfulness. <i>NS: Brief Symptom Inventory.</i>	
Shapiro (2005)	n=38 healthcare professionals randomised to n=18 active; n=20 WL control.	CC analysis. Attrition at 8wk: 44% active, 10% control.	8*2hr weekly MBSR groups, including loving kindness meditation.	Sig. vs WL control: PSS, Self-Compassion Scale <i>NS (trend): Brief Symptom Inventory, MBI, Satisfaction with Life.</i>	
Galantino (2005)	n=84 hospital employees, 96% female. ( <i>uncontrolled</i> )	CC analysis. Attrition at 8wk: 18% active.	8*2hr weekly MBSR adapted for occupational settings to address strategies for balancing work-life balance, work demands + audio CD for home practice.	Sig. changes over time: POMS-SF, MBI emotional exhaustion & depersonalisation. <i>NS: Interpersonal Reactivity Index.</i>	<i>NS: salivary cortisol (1 pre/1 post sample collected 5-7pm by 42 participants).</i>
Davidson (2003)	n=48 biotechnology employees randomised n=25 active; n=16 WL control.	CC analysis. Attrition at 4mth: 15%.	8*2.5-3hr MBSR + 7hr silent retreat + home practice audiotapes 1hr/day, 6days/wk.	Sig vs WL control: Spielberger Trait Anxiety Inventory. <i>NS: PANAS mood, trend for lower NA.</i>	Sig vs WL control: rise in antibody titre in response to flu vaccine post MBSR, EEG increase in left-sided anterior brain activation (related to antibody titre).

Note: WL=wait-list; ITT=intention-to-treat; CC=complete case or per protocol analysis; MM=mindfulness meditation; MBSR=Mindfulness Based Stress Reduction; \*=primary outcome; Sig.=statistically significant effect; NS=not significant association; PSS=Cohen's Perceived Stress Scale; MBI=Maslach Burnout Inventory; CAMS-R=Cognitive and Affective Mindfulness Scale Revised; MAAS=Mindfulness Attention Awareness Scale; POMS-SF=Profile of Mood States Short Form; CES-D Center for Epidemiological Studies Depression Scale; HRV=heart rate variability

## *Results*

The 14 articles described n=8 randomised controlled trials, n=2 non-randomised controlled trials and n=4 uncontrolled interventions. Eight studies involved healthcare workers. Eight studies compared mindfulness training to a wait-list control group only, n=1 to a leadership programme, n=1 to an education programme and n=1 to both yoga and wait-list groups. Half of the studies used an 8-week programme including at least 2-hours of group sessions per week and the remaining seven studies tested shorter programmes. Four studies tested standard MBSR. Eight studies assessed outcomes only directly after the intervention; n=6 studies reported one or more additional follow-up assessments ranging from 3 to 15 months post intervention.

All seven studies which measured dispositional mindfulness as an outcome reported a significant post-intervention increase; n=2 in uncontrolled trials (Schenstrom et al., 2006; Krasner et al., 2009), n=4 compared with a wait-list group (Cohen-Katz et al., 2005; Klatt et al., 2009; Hulsheger et al., 2012; Wolever et al., 2012) and only n=1 compared with an active education control group (Malarkey et al., 2013).

### *i) Positive affect and subjective well-being outcomes*

Nine articles assessed positive affect or well-being outcomes. Mindfulness-based training was associated with significant increases in one or more measures in n=6 studies while n=2 found a similar non-significant trend. A significant increase in the POMS vigour-active scale over time was reported in two uncontrolled studies of healthcare workers (Galantino et al., 2005; Krasner et al., 2009). There were no significant main effects on PANAS positive affect in two small trials (Davidson et al., 2003; Jha et al., 2010), but Jha et al. (2010) did find higher positive affect in those who practiced meditation for longer. Increases in evaluative well-being measures were reported in two randomised controlled trials, including the mental component of the SF-36 scale Health Survey after one year (Mackenzie et al., 2006; Geary and Rosenthal, 2011), and two uncontrolled interventions (Schenstrom et al., 2006; Bazarko et al., 2013). A trend for higher life satisfaction was also reported in a small trial of 38 healthcare professionals (Shapiro et al., 2005). Mackenzie et al. (2006) found a large effect on life satisfaction, but no effect on optimism or job satisfaction in a small sample of nurses. Hulsheger et al. (2012) also found a significant effect on job satisfaction in 22 workers who

completed at least six minutes meditation per day over a two week course, compared with 42 wait-list controls. No studies controlled for effects on negative affect.

#### *ii) Work stress*

Eight studies included a measure of work-specific stress measure: six out of seven studies which measured burnout reported a significant reduction in one or more subscales and one study reported a similar trend (Shapiro et al., 2005). Mindfulness was consistently associated with a reduction in the Maslach Burnout Inventory (MBI) emotional exhaustion subscale, with specific studies also reporting effects on personal accomplishment (Cohen-Katz et al., 2005; Krasner et al., 2009) and depersonalisation (Mackenzie et al., 2006; Krasner et al., 2009). Schenstrom et al. (2006) used a single-item visual analogue scale to assess perceived work stress in 52 healthcare professionals and found a significant decrease sustained three months after a 50-hour mindfulness programme.

#### *iii) Global stress and negative affect*

Eleven out of 14 studies assessed a global measure of stress or negative affect. Two uncontrolled studies reported a reduction in all negative affective subscales of the POMS (Galantino et al., 2005; Krasner et al., 2009) and two randomised trials reported a non-significant trend for lower PANAS negative affect (Davidson et al., 2003; Jha et al., 2010). Mindfulness training was associated with a reduction in Cohen's Perceived Stress Scale in four randomised trials in comparison to a wait-list group and one uncontrolled intervention (Shapiro et al., 2005; Klatt et al., 2009; Geary and Rosenthal, 2011; Wolever et al., 2012; Bazarko et al., 2013). Two randomised trials comparing mindfulness meditation with an active control group found no specific effect of MBSR on PSS, either versus an 8-week education control (Malarkey et al., 2013) or a 12-week yoga intervention (Wolever et al., 2012). In symptom inventory scales which included both perceived mental and physical health, mindfulness interventions were more strongly associated with reduced mental distress than improvements in perceived physical health (Geary and Rosenthal, 2011; Bazarko et al., 2013)

#### *iv) Blood pressure or cardiac outcomes*

Wolever and colleagues (2012) measured blood pressure at a single clinic assessment before and after a 12-week Mindfulness at Work programme. There were no changes over time

within those allocated to mindfulness (n=96) or compared with a wait-list (n=53) or yoga intervention (n=90). There was however a significant increase in heart rhythm coherence from baseline to preparation for a stressful task post-intervention compared with wait-list control for both the mindfulness and yoga arms. Heart rhythm coherence is an indicator of heart rate variability so the increase in this study is thought to reflect reduced sympathetic autonomic reactivity. Geary and Rosenthal (2011) found no effect on pulse rate variability in 59 hospital employees who completed 8-weeks MBSR versus a wait-list control group (n=94), assessed via a resting 5-minute pulse rate measure.

*v) Salivary cortisol*

Klatt et al. (2009) found no effect on salivary cortisol when 24 university staff completed a 6-week 1 hour MBSR programme, compared with a wait-list control group. Samples were taken at three timed intervals from waking over two days, before and after the intervention, and on one day per week during the programme. Malarkey et al. (2013) found no significant group effects on salivary cortisol for 84 staff who completed a similar 8-week programme versus a lifestyle education control group (n=86). Cortisol was sampled at four time-points over three days. Galantino et al. (2005) found no impact of 8-weeks MBSR on a single pre- vs. post-salivary cortisol measure.

*vi) Other biological and cognitive outcomes*

In a workplace trial involving 48 biotechnology workers, Davidson et al. (2003) found that MBSR was associated with a shift in electroencephalographic (EEG) asymmetry toward greater left sided anterior activation, a pattern they reported was indicative of positive emotion. Meditators also generated a stronger antibody response to influenza vaccine than the wait-list group, which was correlated with magnitude of EEG changes. Malarkey et al. (2013) recruited university employees with a raised C-reactive protein (CRP) level, an inflammatory marker associated with an increased risk of myocardial infarction (Wannamethee et al., 2009). There were no significant differences in inflammatory markers (CRP, IL-6) between the mindfulness intervention group and a control group after the two month programme but the CRP level was one mg/ml lower in the mindfulness group. A larger effect on CRP occurred in non-obese employees. Jha et al. (2010) described an intensive 8-week mindfulness programme for soldiers before deployment to combat zones. Higher levels

of mindfulness practice appeared to buffer declines in working memory capacity observed in soldiers deployed without mindfulness training, but there were no overall group effects.

#### *Summary of results and limitations of workplace mindfulness trials to date*

Associations between mindfulness training and the outcomes of interest are summarised in Table 7.3 below.

**Table 7.3 Effects of mindfulness-based workplace programmes: summary**

Outcome category	Specific outcome measures	First author	Effect of intervention
Subjective well-being	SF-12 vitality	Bazarko (2013)	increase (no control group)
	SF-36 mental health	Geary (2011)	increase vs. wait-list control
	POMS-vigour	Krasner (2009)	increase (no control group)
	Satisfaction with life	Mackenzie (2006)	increase vs. wait-list control
	Quality of life	Schenstrom (2006)	increase (no control group)
	POMS-vigour	Galantino (2005)	increase (no control group)
	PANAS PA	Jha (2010)	trend for larger increase with longer practice vs. wait-list control
	Life satisfaction	Shapiro (2005)	trend for increase vs. wait-list control
	Optimism	Mackenzie (2006)	no effect vs. wait-list control
	PANAS PA	Davidson (2006)	no effect vs. wait-list control
Work stress	Burnout (CBI)	Bazarko et al. (2013)	decrease (no control group)
	Burnout (MBI)*ee	Hulsheger et al. (2012)	decrease vs. active control
	Burnout (MBI)	Krasner (2009)	decrease (no control group)
	Burnout (MBI)*ee, dp	Mackenzie (2006)	decrease vs. wait-list control
	Work stress, VAS	Schenstrom (2006)	decrease (no control group)
	Burnout (MBI)*ee, pa	Cohen-Katz (2006)	decrease vs. wait-list control
	Burnout (MBI)*ee	Galantino (2005)	decrease (no control group)
	Burnout (MBI)	Shapiro (2005)	trend for decrease vs. wait-list control
	Burnout (MBI)*pa	Mackenzie (2006)	no effect vs. wait-list control
	Burnout (MBI)*dp	Cohen-Katz (2006)	no effect vs. wait-list control
	Burnout (MBI)*pa, dp	Galantino (2005)	no effect (uncontrolled)
Objective biological/ cognitive markers	HRV under stress	Wolever (2012)	increase vs. wait-list control
	Antibody titre, left EEG	Davidson (2006)	increase vs. wait-list control
	CRP	Malarkey (2012)	trend for decrease vs. active control
	Working memory	Jha (2010)	trend for larger increase with longer practice vs. wait-list control
	CRP, IL-6, cortisol, leptin	Malarkey (2012)	no effect vs. active control
	Blood pressure	Wolever (2012)	no effect vs. wait-list control
	Pulse rate var. (HRV)	Geary (2011)	no effect vs. wait-list control
	Salivary cortisol	Klatt (2008)	no effect vs. wait-list control
	Salivary cortisol	Galantino (2005)	no effect (uncontrolled)

*In 'Effect of intervention' column, 'trend' indicates directional change reported by authors but no statistically significant main effect ( $p > 0.05$ ). 'PA'=positive affect, 'VAS'=visual analogue scale, 'ee'=emotional exhaustion, 'dp'=depersonalisation, 'pa'=personal accomplishment*

Mindfulness-based training in the workplace improved hedonic and evaluative well-being and reduced burnout in the majority of studies. Effects on well-being were sustained for 12

months or more in two studies (Krasner et al., 2009; Gex-Fabry et al., 2011). Effects on positive well-being were not reported in comparison to an active control group, so conclusions cannot be drawn about the specificity of effects. No studies examined experienced affect over the day, eudemonic well-being, ERI or job strain outcomes. There was no evidence that mindfulness meditation influenced salivary cortisol or blood pressure at work.

The quality of study reporting was mixed, making it difficult to compare effects between studies. With the exception of Wolever et al. (2012), results were reported on a complete cases basis, based on participants who provided follow-up data. Two studies failed to report non-completion rates (Davidson et al., 2003; Geary and Rosenthal, 2011). The proportion of enrolees excluded in post-intervention assessments was typically 15%, but ranged up to 78% (Hulsheger et al., 2012). When analyses are limited to those who complete the study, the randomisation element of the study design is lost (Elwood, 2007). Those who experienced a benefit may have been more likely to respond, leading to over-estimates of effectiveness. No studies reported power calculations; studies that reported non-significant trends may be under-powered to detect small effects.

#### *Suitability of mindfulness-based programmes for testing Figure 7.1 hypothesis*

The workplace studies reviewed above offer only partial support for the suitability of mindfulness meditation as an approach to increase well-being. It is unclear whether the effects on well-being were independent of reductions in negative affect. Effects on EMA positive affect were not reported. One workplace meditation trial which measured daily affect was excluded from this review because it taught Loving-Kindness Meditation (LKM), which explicitly aims to evoke warm and tender emotions (Fredrickson et al., 2008a). LKM participants reported higher daily positive emotions over nine weeks compared with a wait-list group and improved life satisfaction after a year, independently of changes in negative affect (Cohn and Fredrickson, 2010). The overt focus on positive emotions during LKM risks increased reporting of positive affect due to increased salience or social desirability effects, but this study does reinforce evidence that meditation training related to mindfulness is a feasible and durable method for promoting well-being at work.

Standard MBSR is a time-intensive programme and lack of available time during work hours may explain some small samples and high rates of attrition. Several studies offered



financial incentives to increase adherence (e.g. Malarkey et al. \$350, Wolever et al. \$150), but this limits the feasibility of expansion to other settings. Several studies adapted programmes to increase accessibility such as by delivering instruction via lunch hour sessions (Malarkey et al., 2013), teleconferences (Bazarko et al., 2013), an online classroom (Wolever et al., 2012) or a self-guided booklet and CD (Hulsheger et al., 2012). All of these studies reported increases in self-reported mindfulness. Wolever et al. (2012) found no differences in outcomes between participants who took part in a face-to-face group versus a remote online classroom. Additional research outside the workplace supports benefits of online mindfulness training. For example, patients with IBS (irritable bowel syndrome) reported symptom improvements up to a year after a 10-week online programme which included only two hours of therapist contact (Ljótsson et al., 2011). Two small-scale pilot studies reported that online-only mindfulness-based training improved mental health (Gluck and Maercker, 2011; Krusche et al., 2012). As noted for PPIs and SMIs, online programmes offer potential advantages over face-to-face programmes in terms of large-scale delivery, standardised delivery, low cost, user convenience and privacy. Computer-based CBT has been found to be as effective as face-to-face therapy for patients with anxiety or depression (Andrews et al., 2010).

It remains unclear how much mindfulness-based training, and of what type, is required to drive improvements in well-being. Most studies in this review reported outcomes after an 8-week group programme but significant gains in mindfulness were reported after as little as six minutes per day of independent meditation practice (Hulsheger et al., 2012). Improvements in life satisfaction were reported after four weekly 30-minute groups, plus independent practice (Mackenzie et al., 2006). A recent meta-analysis found no correlation between outcome effect sizes and mindfulness practitioner contact hours (Carmody and Baer, 2009). Similarly, self-reported measures of meditation practice time do not consistently predict outcomes (Nyklicek and Kuijpers, 2008; Dobkin and Zhao, 2011). The heterogeneity of adapted workplace programmes, which may include yoga or cognitive skills training, also makes it difficult to evaluate the 'active' ingredient. Further research is warranted to clarify the most efficient methods to gain benefits from mindfulness-based training, and the mechanisms involved.

### *Biological outcomes*

Studies in this review suggested that mindfulness-based training had no effect on salivary cortisol, including one large study which measured cortisol over three days at four time points (Malarkey et al., 2013). This is consistent with a randomised controlled trial of MBCT which assessed cortisol in 56 depressed patients repeatedly over one year and found no effect of the intervention (Gex-Fabry et al., 2011). In contrast, one widely cited study reported that MBSR reduced cortisol in 49 cancer patients for up to a year (Carlson et al., 2007). This was an uncontrolled intervention which did not assess cortisol in relation to time of waking. More recently, Jacobs et al. (2013) showed that mindfulness training had no impact on changes in afternoon and evening cortisol over time in 57 healthy adults after an intensive three month mindfulness retreat. However, Jacobs and colleagues did report that dispositional mindfulness was significantly inversely related to mean cortisol both before and after the intervention. It may be that mindfulness-based training does not influence neuroendocrine activity. Alternatively, longer duration studies, a higher frequency and number of salivary cortisol samples or larger participant numbers may be needed to control for normal within-person variability in salivary cortisol (Gex-Fabry et al., 2011). As discussed in section 2.2.3, hair cortisol concentration may prove to be a useful alternative to salivary sampling for assessing changes in chronic systemic cortisol over time (Russell et al., 2012). To date no published studies have described changes in hair cortisol over time in response to a psychological intervention so sensitivity to change is unclear (Staufenbiel 2012).

Blood pressure was assessed by Wolever et al. (2012) based on one clinic measure, which may not be sufficient to detect changes in the daily variation of blood pressure associated with work stress (Landsbergis et al., 2013). A recent trial in Chinese nursing students found an average reduction of 2.2mmHg in systolic blood pressure after a 7-day mindfulness meditation programme versus a relaxation control, but readings were taken directly after meditation so it is unclear whether effects persisted outside the laboratory (Chen et al., 2012). Recent reviews suggest that meditation can be an effective intervention for reduction of blood pressure in hypertensive patients, but the evidence is largely based on studies of Transcendental Meditation (Rainforth et al., 2007; Goldstein et al., 2012).

Interventions using mindfulness-based meditation have shown potential benefits for well-being and the reduction of burnout in the workplace but evidence for specific effects of mindfulness meditation is weak. The duration, format and content of workplace programmes required to effectively enhance well-being is not yet clear. Research examining biological outcomes is at an early stage. Recent trials have reported effects on heart rate variability and a trend for reduced inflammation, but larger trials may be necessary to detect small effects in healthy populations.

### *Workplace well-being intervention selection and design*

In this chapter I presented a hypothesis for the effects of increased well-being on job strain, blood pressure and cortisol. I discussed the pros and cons of different intervention approaches. PPIs can be simple and easy to administer but the effects in working populations are unproven, particularly in terms of biological outcomes (section 7.3). Traditional SMIs may influence well-being indirectly via reduced negative cognitions. Emerging interventions which promote resilience at work offer potential for improving psychological resources, but large-scale workplace trials have not been reported. Biofeedback approaches can influence physiological activation but may be prohibitively expensive for large-scale interventions and may not influence well-being (section 7.4). Mindfulness-based interventions have been associated with increased well-being but effects on blood pressure and salivary cortisol in workplace settings have not been demonstrated to date. Limited evidence from studies outside work settings suggests that well-being improvements are not simply a consequence of reduced stress but arise as a result of improved emotional regulation (section 7.5).

On balance, I decided that a mindfulness-based intervention would offer the most suitable intervention approach to test my hypothesis. To build on the strengths of previous studies and to address some of the limitations identified in this review, I aimed to incorporate the following features into my intervention:

#### Study design:

- A randomised controlled trial (RCT) to compare a mindfulness-based intervention with an active control intervention in order to test the specificity of effects;
- Sample size to be calculated to ensure the study is sufficiently powered to detect changes in the main trial outcome: subjective well-being;

- Intervention to be delivered using online or automated methods, in order to ensure standardised delivery, user convenience, low cost and potential for scaling up.
- Outcomes to be assessed both post intervention and after 6 months follow-up to test sustainability of effects.

#### Outcomes:

- Subjective well-being outcomes to include both experienced affect and eudemonic dimensions of well-being, which have been neglected in studies to date;
- Work stress outcomes to include ERI and job strain measures which have been linked prospectively to heart disease;
- Blood pressure to be assessed using multiple measures over a working day, to reduce 'white coat' effects and improve reliability.
- Changes in cortisol to be measured using hair cortisol concentration, as an indicator of systemic cortisol over several months. Hair cortisol is less influenced by moment-to-moment 'state' influences than salivary samples and has a lower participant burden (Staufenbiel et al., 2013). This will be included as an exploratory measure.

## **Chapter 8 A mindfulness intervention to boost well-being and reduce stress at work**

This chapter describes the design and implementation of a trial which I designed to test the hypothesis that improved psychological well-being would decrease perceptions of job strain and associated physiological activation. Section 8.1 describes the intervention, a mindfulness smartphone application. Section 8.2 describes a pilot feasibility study. Section 8.3 describes the trial, which was conducted in two workplace settings.

### **8.1 The intervention: the Headspace On-the-Go Smartphone App**

I searched for a standardised online mindfulness programme suitable for a healthy working population. I identified Headspace™, a company which provides an online mindfulness programme which was designed to make mindfulness meditation relevant and accessible to modern consumers. I approached Headspace to collaborate in this research in August 2011. Headspace agreed to provide their programme to research participants free of charge. In return I agreed to share anonymised feedback from participants about their experiences of using the app. My role was to design, implement and analyse the research, with responsibility for data integrity.

*The Headspace online programme: [www.headspace.com](http://www.headspace.com)*

The Headspace programme is a self-guided approach to learning mindfulness which consists of a series of guided audio meditations and introductory animations. The content was developed by Andy Puddicombe, a former Buddhist monk and experienced mindfulness trainer. The Headspace approach is unusual because it suggests that benefits from meditation can be achieved from as little as 10 minutes per day of regular practice (Puddicombe, 2011; 2012). New users are not given a written introduction to mindfulness meditation. Instead, they watch a series of short animations (each <2 min long), which explain how to meditate and potential benefits. The content introduces the principles of present moment awareness and nonjudgmental acceptance, which are outlined in section 7.5.1, using visual

metaphors. An example is summarised in Figure 8.1.<sup>17</sup> 'Expectation' explains how mindfulness can lead to feelings of calm by watching thoughts and feelings pass, rather than by actively trying to change them.

**Figure 8.1** Summary of 'Expectation' animation

Animation to introduce new users to the Headspace™ mindfulness programme (www.headspace.com)

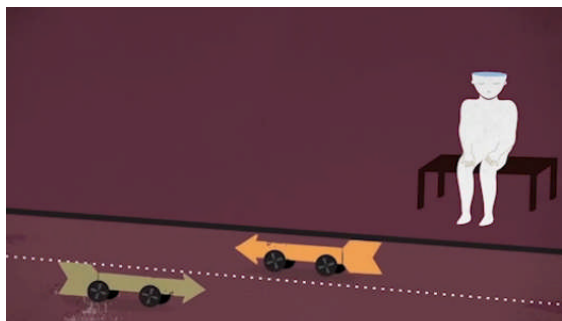
Imagine yourself sat down at the edge of a busy road.

Before you start to meditate it's like having a blindfold on – you're aware of the background noise and stress of the environment, but you're not really able to see what it is that is causing the stress.



When you start to meditate it's like taking the blindfold off. You start to see the thoughts and feelings in your mind. You get to understand why and how you feel the way you do.

The temptation is to run out into the middle of the road, chasing after the pleasant thoughts and running away from the bad ones. But that's really quite exhausting.



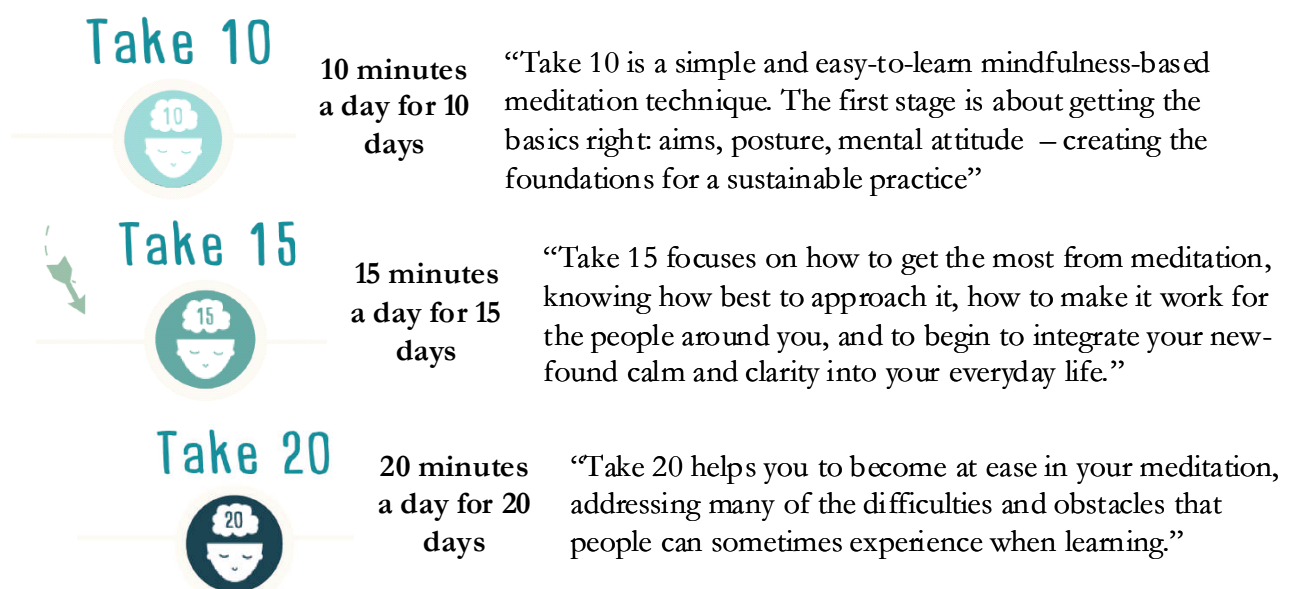
Meditation takes a different approach – it's about holding your seat on the side of the road and watching the autonomous flow of traffic come and go.

When you do that, you'll find that the volume of traffic starts to decrease and the spaces between the cars start to increase. And that's the place of calm and clarity that feels so nice.

<sup>17</sup> <http://www.youtube.com/watch?v=00Xvnz7Lo5o> accessed August 2013

In September 2011, the Headspace programme consisted of a 45-day series of audio podcasts, starting with 'Take 10': ten 10-minute recordings designed to be listened to once each day for ten days. Every session, users listened to the voice of Andy Puddicombe talk them through breathing and body scan exercises designed to cultivate a state of mindful awareness. Users were instructed to sit still in a chair with their feet flat on the floor and to concentrate on counting their breaths, allowing thoughts and emotions to come and go from their consciousness. Each time they became distracted from their breathing, they were instructed to gently bring their attention back to their breathing. Each new day of the programme was unlocked after completing the previous session. Take 10 was followed by 'Take 15', 15 days of 15-minute sessions, and 'Take 20' which consisted of 20, 20-minute sessions. The programme was progressive, with fewer spoken instructions and more time for silent meditation in the later, longer stages. Take 15 encouraged listeners to be aware of their motivations for meditation. Take 20 addressed common barriers to meditation. An overview of the programme, described by Headspace, is outlined below in Figure 8.2.

**Figure 8.2 Overview of the 45-day programme, as described by Headspace**

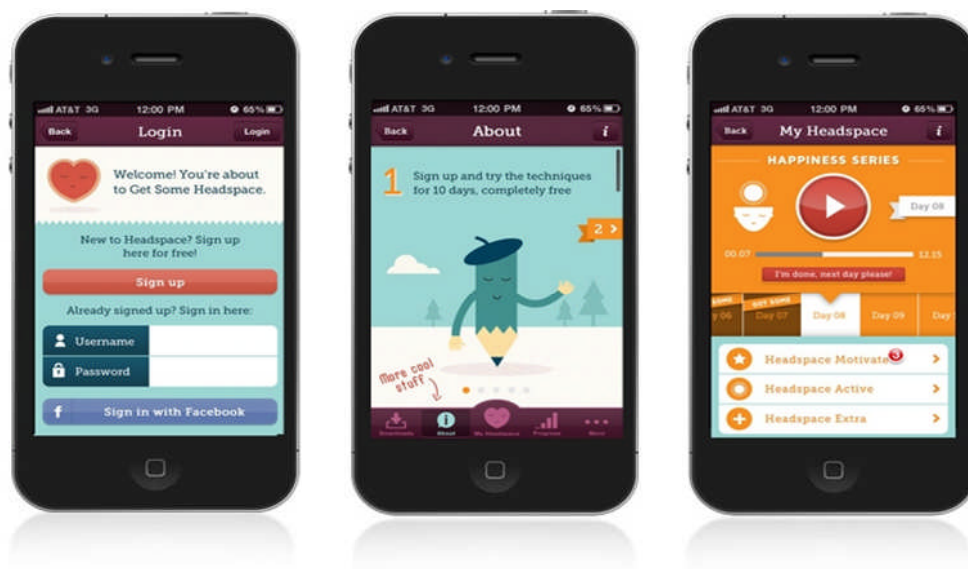


### *A new innovation: the Headspace On-the-go™ App*

Headspace proposed that we evaluate a new 'On-the-go' smartphone application ('the app'), which contained the same content as the online programme. The app enabled participants to listen anywhere by downloading sessions to their phone in advance. The app also provided optional daily reminders. Potential advantages of using smartphones for therapeutic interventions include high global rates of ownership, low cost, routine or regular use, the ability to record and display multimedia information and data input (Ly et al., 2012). No study to date has reported on the use of a smartphone app to deliver mindfulness training but mobile phones have shown potential to enhance psychological treatment in smoking cessation trials (Ehrenreich et al., 2011).

An advantage of the Headspace programme for evaluation was that users were not expected to practice meditation except for listening to recorded sessions; download data captured by the app could therefore be used as an objective measure of meditation practice time. In comparison to standard MBSR, which includes yoga/physical stretches, Headspace used a 'mindfulness-only' approach, based on individual seated meditation. Any well-being benefits associated with the programme could therefore not be attributed to gentle exercise or group interaction (Wolever et al., 2012).

**Figure 8.3** Screenshots of the Headspace On-the-go™ app





## **8.2 Pilot study**

I conducted a pilot study which aimed to assess the feasibility of using the app for a larger workplace trial to improve well-being. The plan was to recruit 40-50 volunteers to use the app for two weeks and to collate feedback on their experiences. Biological outcomes were not assessed in the pilot study.

### **8.2.1 Objectives of the pilot study**

- To test the hypothesis that meditation practice would be positively associated with improvements to psychological well-being and work stress measures;
- To test the functionality and usability of the app for novice meditators;
- To test practical aspects of the research trial including password access to the app and online questionnaires.

### **8.2.2 Pilot study methods**

#### *Recruitment*

Participants were recruited using a combination of convenience and snowball sampling methods (Teddlie and Tashakkori, 2009). I sent a recruitment email to 10 personal contacts, with an invitation to forward to interested friends or colleagues. Recipients who used an iPhone and who were experiencing work-related stress were invited to take part in a two week trial to test a mindfulness meditation app. Interested respondents received a consent form and a hyperlink to an online baseline questionnaire. I created the questionnaires using Opinio software. All respondents who consented and completed baseline questionnaires were recruited. Following the intervention, participants completed a follow-up questionnaire. (Pilot study materials, including questionnaire items, are included in Appendix 8.i-iii).

#### *Measures: primary outcome*

The primary outcome was subjective well-being, assessed using the Warwick Edinburgh Mental Well-being Scale (WEMWBS) (Tennant et al., 2007). WEMWBS was designed to assess general well-being including hedonic (positive mood, energy, clear thinking) and eudemonic (satisfying interpersonal relationships, feeling useful) aspects. All 14-items are positively worded and answered on a 5-point Likert scale ranging from 1 'none of the time' to 5 'all of

the time'. Items are summed to give a score from 14 to 70, with higher scores indicating higher well-being. Psychometric validation in UK population samples found good content validity, reliability and no ceiling affects (Tennant et al. 2007). WEMWBS has been shown to be responsive to change in a wide variety of settings including community centres, schools and psychiatric hospitals and is thought to be suitable for evaluation of interventions at group and individual level (Maheswaran et al., 2012). Cronbach's alpha ( $\alpha$ ) in this study was 0.91, indicating high internal consistency.

#### *Measures: secondary outcomes*

Secondary outcomes were work stress, including social support and overcommitment, and depressive symptoms. Constructs from both the ERI and Demand-Control-Support models (section 4.1.1) were included. Items were extracted from the Whitehall II study questionnaire described in section 5.2 (Bosma et al., 1997; Kuper et al., 2002b; Kuper and Marmot, 2003). Twelve statements were included, including 9-items for job strain (demands 3-items, control 6-items) and 10-items for ERI (effort 4-items, rewards 6-items). (The number of statements was reduced to minimise online questionnaire length. Using data from Chapter 5, ten statements which were very highly correlated ( $r > 0.75$ ) with similar statements within the same subscale were excluded. Included statements are listed in Appendix 8.iii). Each statement was scored on a 4-point frequency scale from 1 to 4. Job strain (demands divided by control) and ERI (effort divided by rewards) were included as ratios based on the mean score per item. Cronbach's alpha ranged from 0.63 for demands to 0.81 for rewards. Low job control and high demands, job strain and ERI indicated higher work stress.

Social support was assessed using 5 statements, such as 'There is a pleasant atmosphere at my workplace' and 'I have a good relationship with my line manager(s)'. Individual items were scored from 1 'strongly agree' to 4 'strongly disagree' and mean scores were computed. Higher scores indicated greater support at work. Low social support based on this scale was linked to raised heart rate and systolic BP in a 24-hour ambulatory monitoring study (Unden et al. 1991). Cronbach's alpha was 0.80.

Overcommitment, which is characterised by an inability to withdraw from work commitments, was assessed using 5-items, such as 'I get easily overwhelmed by time pressures at work'. Statements were scored on a 4-point scale from 1 'strongly disagree' to 4

'strongly agree'. Items were summed, range 5-20, with higher scores indicating higher overcommitment. The scale has previously been linked to elevated cortisol and systolic BP over the day (Steptoe et al., 2004) and heightened sympathetic drive (Vrijkotte et al., 2004). Cronbach's alpha was 0.81.

Depressive symptoms were assessed using an 8-item version of the Centre for Epidemiological Studies Depression Scale (CES-D) (Radloff 1977). Respondents were asked how often in the past two weeks they had 'felt lonely' or 'felt you could not get going', on a scale from 0 'none of the time' to 3 'all, or almost all of the time'. Items were summed, range 0-24, with higher scores indicating higher depressive symptoms. Cronbach's alpha was 0.84.

#### *Measures: process measures*

To check the fidelity of the intervention, mindfulness was assessed briefly using 7-items from the 14-item Freiburg Mindfulness Inventory representing the thoughts, attitudes and experiences related to the concept of mindfulness (Walach et al., 2006). Items included 'I am open to the experience of the present moment' and 'I see my mistakes and difficulties without judging them'. Answers were given on 4-point rating scale ranging from 1 'rarely' to 4 'almost always'. Since a cut-down version of the scale was used, mean scores were computed. Higher scores indicate greater mindfulness. Cronbach's alpha was 0.74. At follow-up, participants were asked how frequently they had used the app and how much time in minutes they had spent meditating over the previous two weeks. Optional open questions were included to probe why participants had not downloaded the app, or stopped using it, any changes they had noticed since they started meditating and suggestions to improve the app.

#### *Additional measures*

Background measures to describe the sample included age, sex, occupation, work full-time/part-time and perceived seniority at work on a scale from 1 'most junior' to 10 'most senior'. Job roles were grouped into three groups (student/ full-time work/part-time work). As a potential predictor of meditation practice and outcomes, participants were asked how confident they were on a scale from 1 'not at all' to 5 'very confident' that they would find time to meditate every day. Using the same scale, they were asked to indicate how confident they were that meditation would make a difference to how they felt about work. Mean scores for these self-efficacy items were computed.

### Planned protocol and amendments

During the three week recruitment phase, 53 people with an iPhone and 13 people without an iPhone expressed an interest in the study. I had planned to exclude iPhone non-users but Headspace agreed that we could include these volunteers as an untreated wait-list control group. They were given access to the Headspace programme online after the pilot study. Fifty-one iPhone users and 11 iPhone non-users completed consent forms and baseline measures.

The app was due to be released on 6th January 2012. Recruitment was completed in November 2011 and participants completed baseline questionnaires in early December, to allow for a typical 'last two weeks' during work time before Christmas (Figure 8.4). These timings were chosen so that the pilot could be completed in advance of the workplace trial. Technical problems delayed the commercial approval of the app. After a two week delay, I sent iPhone users instructions to access Take 10 online. A further week later, a beta version of the app was approved and participants were emailed app download instructions. Unfortunately the beta version did not capture objective download data. Participants were invited to complete an online follow-up questionnaire three weeks later. Participants with an iPhone therefore had the opportunity to meditate for up to four weeks by using the website and app (Figure 8.4).

**Figure 8.4** Planned and actual pilot study timing

	December			January			February			March	
<b>Plan</b> App n=50	Baseline qre										
			Christmas								
					App access						
						Follow-up qre					
<b>ACTUAL</b> App n=51 at baseline	Baseline qre										
			Christmas								
					Delay to app						
						Online access					
						App access					
									Follow-up qre		
<b>ACTUAL</b> Waitlist n=11 at baseline	Baseline qre										
			Christmas								
									Follow-up qre		

### Statistical analysis

Only participants who provided follow-up data were included in analysis of the pilot study. Continuous baseline variables approximated a normal distributed. Characteristics of the

intervention and wait-list control groups at baseline were compared using Chi-squared for categorical variables and independent t-tests for continuous variables. Correlates of dispositional mindfulness were investigated using Pearson correlations. Change scores were calculated to illustrate change in outcomes within each group. The effect of the intervention on outcome variables effects was calculated using repeated measures ANOVAs with time (baseline and follow-up) as the within-subjects factor and treatment group (app intervention versus control) as the between-subjects effect. Meditation time was skewed so Spearman's rank correlations ( $r_s$ ) were used to test associations between outcome measures and meditation time. Group by time interactions were re-calculated using meditation time (in three categories) as the between-subjects factor. Analyses were conducted using SPSS version 18.0.

### **8.2.3 Pilot study results**

#### *i) Baseline characteristics*

Follow-up measures were completed by 42/51 (82%) iPhone users (app group) and 10/11 (91%) non-users (control group). The 10 non-responders all worked full time and were more likely to be men ( $n=8$ ). Attrition was not predicted by baseline well-being, work stress, self-efficacy for practice or anticipated treatment effectiveness. Participants worked in a wide range of occupations including commercial management or analytical roles ( $n=14$ ), engineering ( $n=7$ ), research ( $n=6$ ), teaching ( $n=4$ ), medical ( $n=4$ ), administration ( $n=4$ ) and full-time education ( $n=3$ ). At baseline, depressive symptoms were significantly higher in the app group ( $t=-2.03$ ,  $p=0.048$ ) (Table 8.1).

**Table 8.1 Baseline characteristics of pilot study participants**

	App group n=42	Control group n=10	Between groups difference, p value
<i>Socio-demographic</i>			
Age	33.7 (10.5)	40.1 (11.3)	0.950
Female, %	69.0	60.0	0.584
Work full time, %	78.6	60.0	
Work part time, %	14.3	40.0	
Student, %	7.1	0	0.145
Seniority (0-10)	4.46 (2.3)	5.30 (1.9)	0.574
<i>Psychosocial factors</i>			
Well-being	47.0 (9.0)	50.0 (6.0)	0.329
Job strain	0.63 (0.2)	0.53 (0.2)	0.102
Effort-reward imbalance	0.76 (0.2)	0.69 (0.2)	0.208
Social support	3.21 (0.53)	3.08 (0.51)	0.481
Overcommitment	7.59 (3.47)	5.60 (3.1)	0.102
Depressive symptoms	8.90 (4.5)	5.80 (3.4)	0.048*
Mindfulness	2.24 (0.50)	2.16 (0.62)	0.638

\* indicates  $p < 0.05$ , a statistically significant difference

#### ii) Changes in outcome measures by treatment group

Overall differences over time within each group were small (Table 8.2). In repeated measures ANOVAs and there was only one significant difference between the app and control groups: overcommitment fell from  $7.6 \pm 3.5$  to  $6.3 \pm 3.6$  in the app group and increased from  $5.6 \pm 3.1$  to  $6.2 \pm 2.6$  in the control group ( $F=5.858$ ,  $p=0.019$ ). (There were also no significant interactions with demands, control, effort and reward subscales, not shown in Table 8.2.).

Standard deviations for change scores were larger in the intervention group, despite the larger sample size, indicating wider variability. For example, changes in well-being scores ranged from -5 to +5 in the control group and -15 to +21 in the app group. I therefore investigated the difference in changes over time by meditation practice.

**Table 8.2 Pilot study change scores by treatment group (follow-up – baseline) and repeated measures ANOVAs**

	Treatment group n=42	Control group n=10	Group*time, F-statistic (1,50)	Group*time, p value
	Change scores, mean (SD)			
Well-being	1.36 (8.2)	-1.00 (3.8)	0.78	0.380
Job strain	0.014 (0.15)	-0.004 (0.10)	0.13	0.724
ERI	0.038 (0.15)	0.011 (0.10)	0.21	0.652
Social support	-0.026 (0.34)	-0.060 (0.45)	0.07	0.792
Overcommitment	-1.31 (2.3)	0.60 (2.2)	5.86	0.019*
Depressive symptoms	-1.43 (2.2)	-0.20 (2.7)	0.76	0.387
Mindfulness	0.10 (0.43)	0.16 (0.12)	0.23	0.636

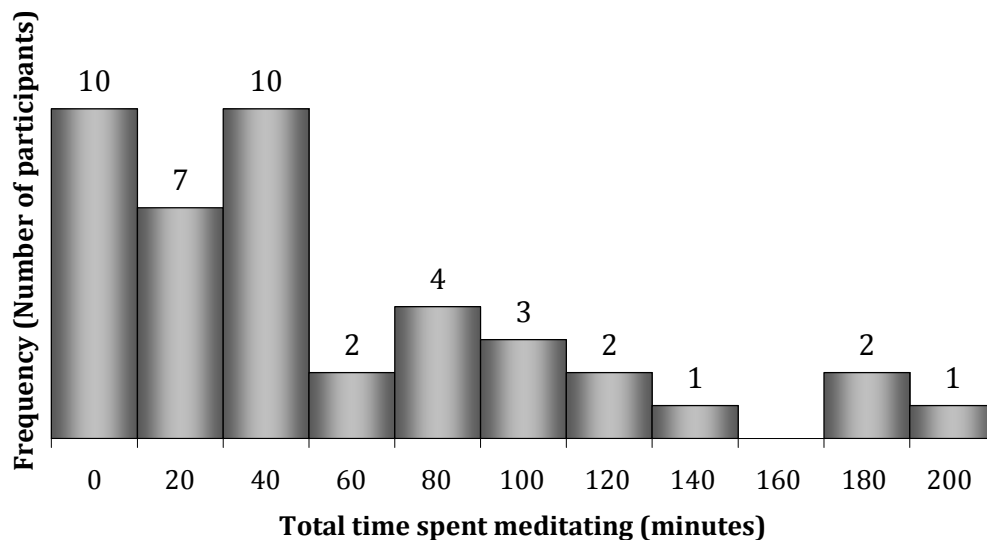
\* $p < 0.05$

*iii) Self-reported meditation practice time*

Although all members of the intervention group were sent instructions to access the online meditation programme on the same day, the total time participants claimed to have spent listening to guided meditation over the 3-4 week intervention period ranged widely from 0-200 min, mean  $49.2 \pm 53$  min (Figure 8.5).

**Figure 8.5 Pilot study self-reported meditation time**

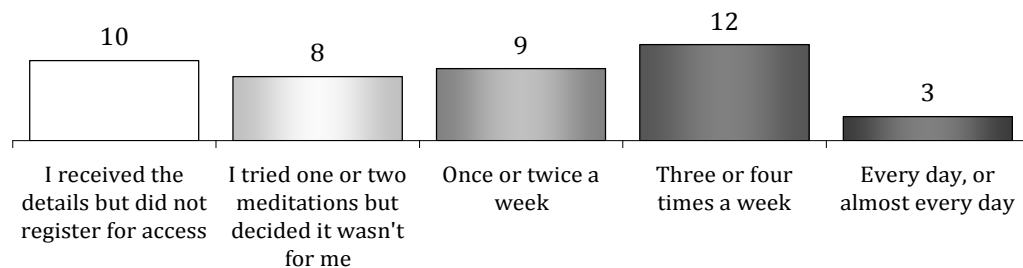
Since the trial began, how much time have you spent listening to the mindfulness meditation programme? (n=42)



Ten participants did not use the programme. Of these, n=2 had not downloaded the app because it was only compatible with iPhone 3GS and above. Others cited time pressures or

forgot: “I just couldn’t find the time to get started”, “To be honest, I just kept forgetting”, “Too busy sadly and emails get lost.” Thirty-two participants accessed the app, of whom n=24 listened at least once a week and n=8 said it wasn’t for them (Figure 8.6).

**Figure 8.6 Pilot study self-report meditation frequency**  
Over the last three weeks, how often have you listened to the meditation programme?



*iv) Did meditation practice time predict changes in well-being and work stress?*

Within the intervention group, time spent listening to the Headspace programme was positively correlated with increases in well-being ( $r_s=0.39$ ,  $p=0.011$ ), mindfulness ( $r_s=0.31$ ,  $p=0.045$ ), social support ( $r_s=0.48$ ,  $p=0.002$ ) and job control ( $r_s=0.32$ ,  $p=0.042$ ). There were no differences in meditation time for those who used only the app ( $n=14$ ) compared with those who used the app and the website ( $n=8$ ).

Baseline characteristics of participants who did not start the programme did not differ from the control group at baseline, so these participants were grouped together into a ‘no meditation’ category to test the effect of no practice vs. low vs. high practice time. Results of repeated measures ANOVAs with practice as the grouping variable (none,  $n=20$  / <1 hr,  $n=18$  / >1hr,  $n=14$ ) are presented in Table 8.3 and illustrated in Figure 8.7. There were significant interactions between practice time and well-being, social support and job control only ( $p<0.05$ ). Effect sizes were highest for well-being, for which the group by time interaction explained 14.7% of the variance, a small effect.

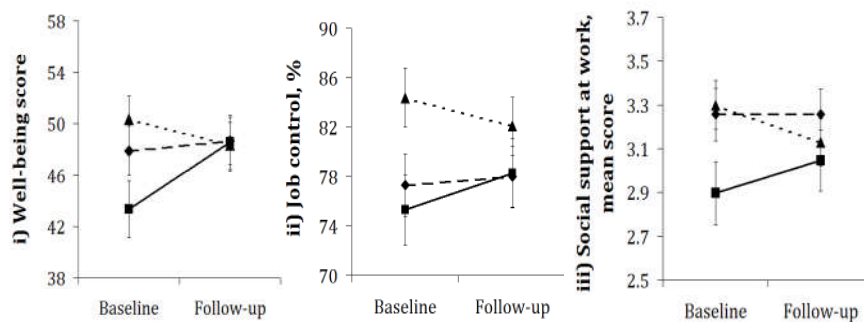


**Table 8.3 Pilot study group (time spent meditating) by time (baseline/follow-up) interactions in repeated measures ANOVAs**  
F statistic, p value and effect size (partial eta-squared ) for group by time interaction

	Group*time, F(2,49)	p value	Effect size ( $\eta^2$ )
Well-being	4.24	0.020*	0.015
Mindfulness	2.75	0.074	0.010
Depressive symptoms	1.37	0.264	0.005
Job control	3.70	0.032*	0.013
Job demands	1.23	0.300	0.005
Job strain	1.79	0.178	0.007
Social support	3.35	0.044*	0.013
Effort-reward imbalance	0.81	0.452	0.003
Overcommitment	2.36	0.105	0.009

\* $p < 0.05$

**Figure 8.7 Pilot study changes in well-being, job control and social support**  
No meditation (▲ dotted line), up to 1 hour (◆dashed line), 1 hour plus (■full line)



v) Did baseline values predict meditation practice time?

At baseline most participants were confident they would find 10 minutes per day to meditate (on a 1-5 'not at all' to 'very confident' scale, mean score  $4.2 \pm 0.6$ , range 3-5). Confidence that practising meditation would influence their feelings about work was lower (mean  $3.2 \pm 0.8$ , range 1-5). Neither of these factors predicted with practice time ( $r_s < 0.20$ ,  $p > 0.1$ ). Time spent meditating was positively associated with higher baseline levels of overcommitment ( $r_s = 0.33$ ,  $p = 0.036$ ) and ERI ( $r_s = 0.37$ ,  $p = 0.019$ ) and negatively associated with baseline well-being ( $r_s = -$

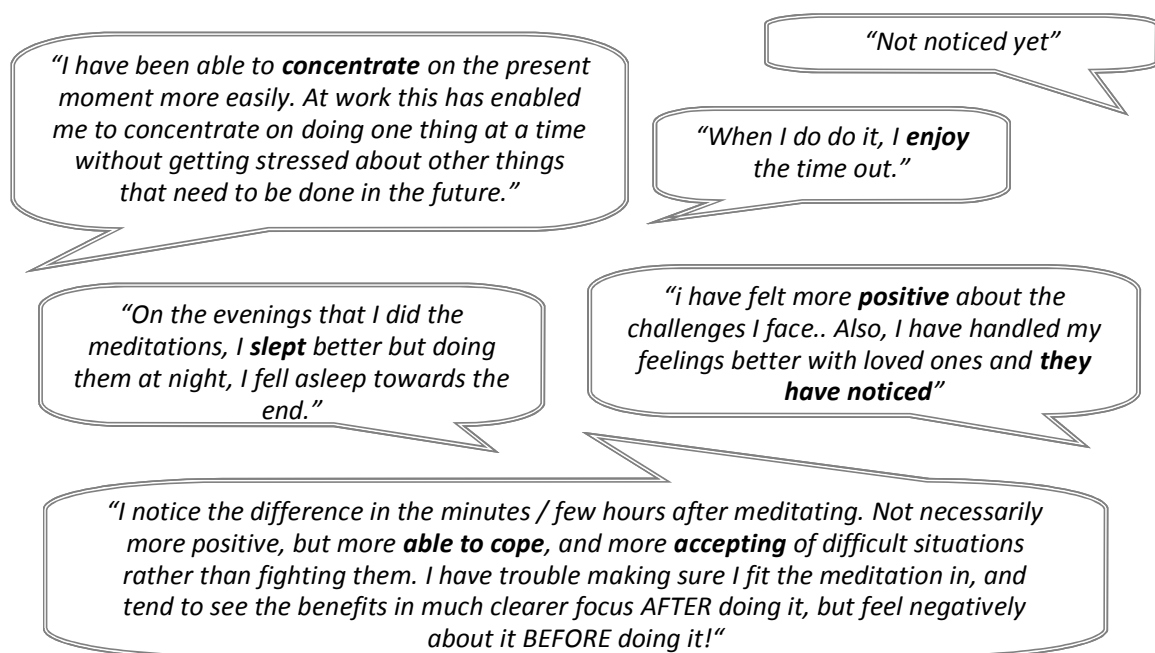
0.34,  $p=0.029$ ), mindfulness ( $r_s=-0.34$ ,  $p=0.029$ ) and social support ( $r_s=-0.42$ ,  $p=0.006$ ). Age was not correlated with practice time but more senior employees reported less meditation ( $r_s=-0.35$ ,  $p=0.024$ ).

#### vi) Feedback about the Headspace programme

Twenty-seven (84%) of the 32 participants who had accessed the programme said that they would recommend Headspace mindfulness meditation to a friend. Twenty out of 24 participants (83%) who meditated at least once a week said that they intended to continue meditating beyond the end of the trial. Participants who had accessed the programme whether they had noticed any changes to the way they felt, positive or negative (Figure 8.8). Several participants mentioned feelings of calmness and relaxation straight after meditating, four in relation to improved sleep. Three said they had more confidence to cope with challenges, three had experienced greater positivity, and two participants commented on improved relationships. Several participants spontaneously mentioned the difficulty of finding time to meditate. Four out of 32 participants (13%) stated that meditation had made no difference to them.

**Figure 8.8** Pilot study qualitative feedback

Has starting mindfulness meditation made any difference to the way you feel? Please tell us a bit about any positive or negative changes you've noticed (Free text)



When asked to suggest improvements to the programme, four participants mentioned that the app reminders to meditate were annoying. Several people also felt that there was too much talking in the Take 10 programme, and that there needed to be more time for silent reflection. Only one of the eight participants who stopped meditating criticised the programme, finding it *“intrusive and irritating”*. Others felt that they too rarely had the time, particularly not during the working day: *“I couldn't find the time in the working day to listen in my office. Putting headphones in and closing my eyes just isn't practical so I found it tricky to do.”*

#### **8.2.4 Discussion: implications of the pilot study**

The pilot study suggested that the smartphone app is a feasible delivery method for mindfulness meditation training. Although overall effects of the intervention on well-being were not significant, mean practice time was only 49 minutes. As hypothesised, longer meditation time predicted larger increases in well-being. The pilot study provided learning in terms of procedures and attrition, and potential for effectiveness.

##### *Effectiveness*

The pilot study was limited by recruitment of a small convenience sample, non-random allocation to treatment group, use of an inactive wait-list control group and technical delays. Reduced item versions of the work stress and mindfulness measures were used, which have not been validated. Despite these limitations, meditation time predicted increased well-being in the hypothesised direction. Meditation time was also associated with gains in job control and social support. Figure 8.7 highlighted that those who meditated for longer had lower baseline scores, so changes may simply reflect regression to the mean effects (Barnett et al., 2005). Alternatively it may be that those with lower well-being at baseline experienced greater benefits and were therefore motivated to engage in greater practice. In the main trial I selected participants with higher work stress at baseline to give more scope for effects to emerge. The delays to launching the app meant that other factors may have influenced outcomes in addition to the intervention. Positively, participants' verbatim comments suggested that the majority of users perceived benefits.

### *Procedures and measures*

Feedback about the app from users was very positive. There were no complaints about app usability or technical failures, although we could not discount that problems had deterred non-respondents. Data collection via online baseline and follow-up questionnaires functioned well. The pilot study relied on self-reported meditation practice time but use of objective download data was planned for the trial.

Measures of well-being, mindfulness, social support and job control were all positively correlated and may have been responsive to meditation (or influenced by regression to the mean). Constructs from the ERI model of work stress did not significantly correlate with changes in mindfulness or well-being and may be more strongly associated with stable work environment factors. Several users mentioned improvements in sleep quality in their verbatim comments so in the interests of space, I decided to remove the ERI work stress scales and add the Jenkins Sleep Scale (Jenkins et al., 1988) to the trial questionnaire. Qualitative feedback regarding confidence and coping also suggested that anxiety may be an important outcome, so I replaced the CES-D with the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983). To try and account for the effects of changing workload, I decided to measure estimated work hours in the main trial.

### *Practice time and attrition*

The pilot study highlighted attrition and non-adherence as key issues. Nine participants in the intervention group were lost to follow-up (18%). Only 32/42 (76%) of respondents to the follow-up questionnaire used the app; if non-respondents are included this is equivalent to only 63% of the intervention group. Meditation time predicted improvements to well-being, job control and social support, suggesting that regular use of the app could optimise the effects of the intervention. Interestingly self-efficacy did not predict practice time but this may be owing to the unexpected delay to app launch, which may have left participants unprepared to start the intervention. In an attempt to improve compliance in the main trial, study dates were publicised in advance of enrolment. I met all participants face-to-face. A lunchtime launch event with Andy Puddicombe was introduced to try and increase motivation to meditate. I also emailed a weekly reminder to participants during the intervention to

encourage continued involvement. The trial duration was extended to 8 weeks, in line with the standard MBSR programme.

### **8.3 A randomised controlled trial to improve well-being at work**

While the pilot study was in progress, I applied to UCL ethics committee for approval of a randomised trial to examine the effects of a mindfulness smartphone app on well-being in the workplace (3035/002). I registered the trial on ClinicalTrials.gov, reference NCT01661569.

The original proposal was for a three-arm trial with an intervention group (Headspace app), an inactive wait-list control group and a relaxation (active control) group. The relaxation control was intended to be a series of calming music podcasts delivered with an app interface similar to the active intervention. Unfortunately delays to the active intervention app meant that Headspace were unable to develop the active control version. At the time the trial was designed (December 2011), I could not identify a suitable alternative control app so the intervention was compared with an inactive wait-list group in a two-arm trial. I initially intended to conduct the trial at one company but extended this to a second site to check the consistency of effects. Time constraints imposed by the first company meant that outcomes were assessed immediately post-intervention and after three months only, rather than post-intervention and six months later. Three month follow-up measures were assessed online, rather than at interview, to minimise worksite disruption.

The trial is described below, based on the CONSORT guidelines for reporting parallel group randomised trials (Schulz et al., 2010).

#### **8.3.1 Aims and hypotheses**

As outlined in Chapter 7, the rationale for conducting the trial was to test the hypothesis that deliberately increasing psychological well-being without making changes to the work environment would reduce perceptions of job strain. The aims of this randomised controlled trial were twofold: firstly, to use a mindfulness meditation smartphone app to improve subjective well-being in healthy but stressed office workers; secondly, to investigate the associations between increased subjective well-being and job strain, blood pressure and cortisol.

The primary trial outcome was psychological well-being. Secondary outcomes included job strain, blood pressure and hair cortisol concentration. Hypotheses were tested on outcomes immediately post intervention (T2), eight weeks after the intervention group were given access to the app. A priori hypotheses were as follows:

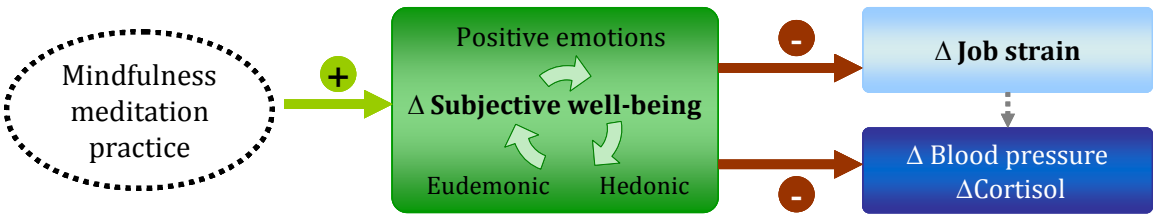
- Hypothesis 1: Participants randomised to the meditation app will show greater improvements in well-being (WEMWBS) and positive affect over the day than those allocated to the wait-list control condition.



- Hypothesis 2: Compared with those allocated to the wait-list condition, app participants will show appropriate changes in secondary outcomes. These are decreased job strain, blood pressure and hair cortisol concentration; decreased negative distress (anxiety, depressive symptoms, negative affect over the day) and increased mindfulness.



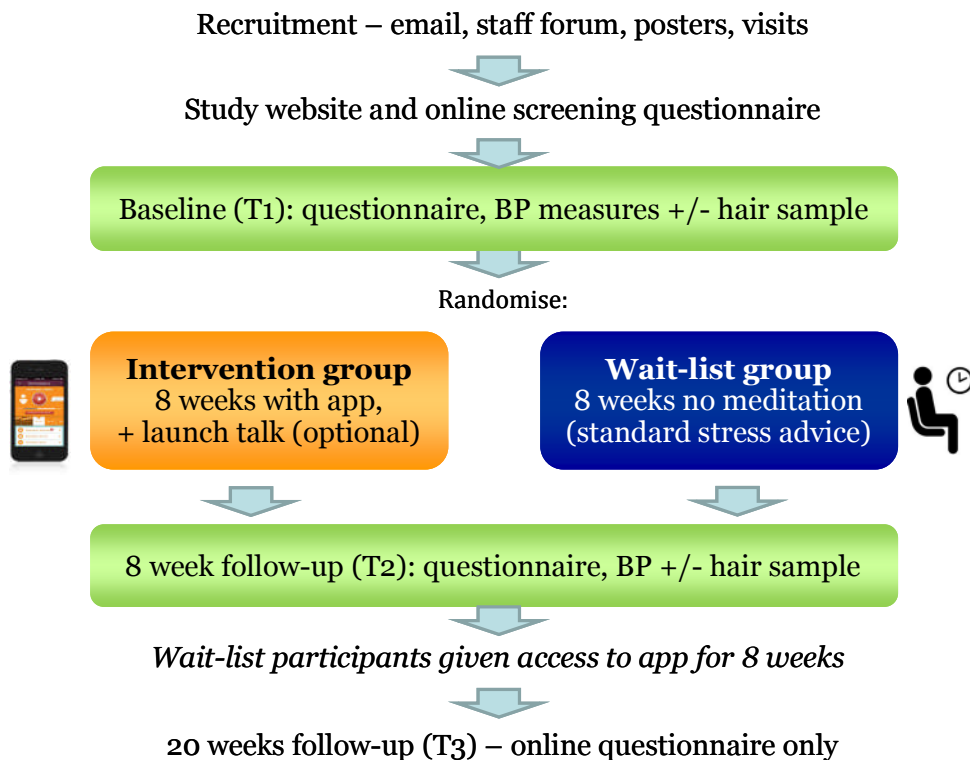
- Hypothesis 3: Longer meditation practice time, based on download data from the app, will be associated with stronger intervention effects on well-being and secondary outcomes in the hypothesised directions.
- Hypothesis 4: Increases in subjective well-being will mediate the effects of the mindfulness intervention on job strain, blood pressure and cortisol. These effects will be independent of changes in negative affect.



### 8.3.2 Methods

The experimental design was a randomised parallel wait-list controlled trial (Figure 8.9). All outcome measures were assessed at baseline (T1) and eight weeks later (T2, immediately post intervention). Wait-list participants could download the app directly after their T2 interviews. Psychological outcomes were re-assessed 8-10 weeks later (T3), to explore the sustainability of changes in well-being (WEMWBS).

**Figure 8.9** Outline trial protocol



#### Sample Size

A meta-analysis of studies using MBSR in healthy people reported an effect size Cohen's  $d=0.74$  for stress reduction across 7 controlled studies (Chiesa and Serretti, 2009). In clinical populations, a meta-analysis found a pre-post effect size estimate of  $d=0.59$  for improved mood across 39 studies (Hofmann et al., 2010). The current study was powered to detect changes in the primary outcome, well-being. A power analysis indicated that to detect a standardised difference of 0.59 with 80% power using a cut-off for statistical significance of 0.05, two groups of  $n=46$  would be needed (Whitley and Ball, 2002). The pilot study found 18% attrition in the intervention group after a 4-week meditation intervention and 9% in the

wait-list group. I aimed to recruit a minimum of  $n=55$  in each group at each site; up to 10 further participants were allocated to the intervention group, to allow for higher attrition (up to 29% at 8 weeks).

### *Participants*

Participants were office workers recruited from two large UK companies, Site A and Site B, described below. At each site, employees were invited to participate in a research trial using a smartphone app to tackle work stress and enhance well-being. Interested employees were referred to a study website, [www.wellbeingapp.info](http://www.wellbeingapp.info), which contained the study information and access to a screening questionnaire (Appendix 8.iv-vi). To avoid medical treatment influencing outcomes, employees receiving treatment for depression, hypertension or heart disease were excluded ( $n=40$ ). Other criteria for exclusion were: not having a smartphone ( $n=19$ ), refusing to accept random allocation to the intervention or a wait-list control group ( $n=11$ ), practising mindfulness meditation more than once a week ( $n=0$ ). To avoid floor effects for work stress, only respondents scoring one or more on the 6-item work overcommitment scale (Kuper et al., 2002b) were eligible. This measure was described in section 8.2. Respondents were asked to leave their email address for re-contact by the researcher.

### *Site A*

Site A was the headquarters of a UK pharmaceutical firm with approximately 900 onsite employees working across a wide range of functions including research and development, marketing and sales, people management, IT support and administration. The ratio of female to male employees was 2:1. Recruitment was via an invitation email to all staff and posters displayed on large screens in public areas (Appendix 8.iv). I also organised a stand outside the staff canteen during one lunch hour to answer questions and raise awareness of the study.

### *Site B*

Site B was a high-tech company. Over 1500 employees were based across three office buildings in London. Employees worked across a range of business functions broadly categorised into engineering, sales or general and administrative roles. Recruitment was via an advert on the online staff notice board, posters in public areas and a lunch hour visit to each office to raise awareness of the opportunity to participate in the study.



### *Procedure*

Three weeks were allocated for recruitment at each site. Eligible participants were contacted in a random order (using a random number generator) and invited to choose an appointment time until a maximum of 120 baseline appointment slots were filled. Interviews were conducted over three weeks on working days, excluding Fridays, to ensure that blood pressure readings were completed during the working week.

At the baseline interview, (T1) participants were asked to read the study information sheet and given the opportunity to ask questions before giving signed consent. Height and weight were measured for the assessment of BMI. Participants completed the study questionnaire online and were then instructed how to use the blood pressure monitor. It was explained to participants that measuring changes in hair cortisol concentration over time was an exploratory technique, without benchmark data, and therefore hair samples were optional.

Participants were allocated a study number and randomised to the app group or wait-list group using a random number generator.. All those allocated to the app group received instructions to download the Headspace On-the-go app and an access code which gave them free access to the 45-day programme. The app group were also invited to an optional one hour introductory talk about mindfulness meditation by Andy Puddicombe, held onsite during the working day. The talk was based on content from the app, including the introductory animations and a 10-minute guided meditation. Users were asked to listen to a maximum of one mindfulness podcast each day. A reminder to meditate was sent via email once a week.

Wait-list control participants were told that they would start the intervention after their 8-week follow-up interview. In the intervening period, they were advised to read the tips for reducing work stress on the NHS website<sup>1</sup> but asked not to start meditating. Anyone needing urgent help to cope with stress was directed to their line manager, or to a confidential Employee Assistance Programme phone number.

Participants were encouraged to schedule T2 follow-up interviews on the same day of the week and the same time of day as their baseline appointment where possible, to minimise

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<sup>1</sup> <http://www.nhs.uk/Livewell/workplacehealth/Pages/beatingworkstress.aspx> accessed March 2012

the influence of time of day to variations in mood (Dockray et al., 2010). Follow-up interviews used the same protocol as baseline interviews but weight and height measures were not repeated. After the follow-up interviews, wait-list condition participants were given access to the app and invited to the same introductory talk as the first app group. A brief online questionnaire to assess well-being (WEMWBS), job strain and app feedback was circulated a further 8 weeks later (T3) and completed within two weeks.

### *Measures*

The primary outcome was subjective well-being assessed by two measures. Firstly, the Warwick Edinburgh Mental Well-Being Scale (WEMWBS) assessed retrospective eudemonic and hedonic well-being over the past two weeks. This measure was used in the pilot study and is described in section 8.2.2 above. Secondly, positive affect over the day was assessed using an ecological momentary assessment (EMA) approach by asking participants to rate their current mood at five timed intervals over the day (06:30-08:30 / 11:00-12:00 / 16:00-17:00 / 19:00-20:00 / 22:00-23:00). Six emotions were rated on a 5-point scale from '1' don't feel this way at all to '5' feeling is extremely strong (Appendix 8.x). Positive affect was calculated as the mean of ratings for 'happy', 'relaxed' and 'interested or engaged' over the day, in order to capture both high and low arousal positive emotions. In the results, unless otherwise specified, 'well-being' refers to WEMWBS scores and 'positive affect' to EMA ratings.

Secondary psychological outcomes were job strain, general psychological distress (negative affect over the day, anxiety and depressive symptoms), sleep problems, social support at work and mindfulness. Job strain was assessed using the Whitehall II Job Characteristics Questionnaire (Bosma et al., 1997), described in Chapter 5 (section 5.2). As in Chapter 5, job strain was calculated as a continuous score based on the quotient approach (job strain = mean demands/ mean control). Separate demands and control scales were also converted to percentage scores for comparison with studies described in chapters 5 and 6. Negative affect over the day was based on mean mood ratings for 'angry or irritated', 'sad or upset' and 'anxious or worried' which were recorded at the same times as positive affect. The Hospital Anxiety and Depression Scale (HADS) is a 14-item scale with separate items for generalised anxiety (HADS-A, 7-items) and depression (HADS-D, 7-items) (Zigmond and Snaith 1983). The scale was developed to assess mental distress and avoid reliance on somatic symptoms such as fatigue. Respondents rated each item on a scale from '0' absence to '3'

extreme presence with scores summed with a range 0-21, with higher scores indicating higher distress. Although originally developed for use with hospital patients, the HADS has been validated in general population samples (Bjelland et al., 2002).

Sleep problems were assessed using 4-items from the Jenkins Sleep Scale (Jenkins 1988) which was described in section 5.2. Mean scores were computed with higher scores indicating more sleep problems. Social support at work was assessed with the scale devised by Unden et al. (1991) which was used in the pilot study (section 8.2.2). Higher scores indicated a better work environment, strong group cohesion, high quality relationships between colleagues. Mindfulness was assessed with the full 14-item Freiburg Mindfulness Inventory, as described in section 7.5. Items measured the thoughts, attitudes and experiences related to the concept of mindfulness (Buchheld et al., 2001; Walach et al., 2006).

Biological outcomes were blood pressure and hair cortisol concentration. Workers experiencing job strain tend to show raised blood pressure during the working day and evening (section 4.2.1)(Landsbergis et al., 2013). Participants were trained to measure their blood pressure using an Omron R2 wrist monitor which has been validated for self-measurement by the European Society of Hypertension (Topouchian et al., 2011). Wrist monitors were used because they are smaller and lighter than upper arm cuffs and participants were asked to carry the monitor for 24 hours. Participants were asked to write down two readings, taken 3 minutes apart, at the same five time intervals when they rated their mood (Appendix 8.x). All readings were averaged to give a single mean value for systolic and diastolic BP. Blood pressure can vary widely during the diurnal cycle (Vrijkotte et al., 2000), therefore at T2 individual readings which could not be matched to a reading taken at the same time interval at T1 were excluded.

**Table 8.4 Summary of RCT measures**  
(see Appendix 8.viii for full questionnaires)

Scale	Example items and scoring (Cronbach alpha)
Primary outcomes	
Well-being, Warwick Edinburgh Mental Well-being Scale (WEMWBS)	14 positively worded items. In the last 2 weeks.. 'I've been feeling good about myself', 'I've been feeling interested in other people', 'I've been dealing with problems well'. <i>Rated on a frequency scale from 1 to 5, range 14-70 (<math>\alpha=0.86</math>)</i>
Positive affect (PA) over a working day and evening*	PA = happy/ relaxed/ interested or engaged <i>Emotions scored 1-5 at 5 timed intervals over a working day and evening, mean score range 1-5 (<math>\alpha=0.76</math>)</i>
Secondary psychological outcomes	
Job strain, from the Whitehall II questionnaire	Demands: 'Do you have to work very intensively?', 'Do different groups at work demand things from you that you think are hard to combine?' Control: 'Do you have a choice in deciding HOW you do your work?' <i>Rated on a frequency scale 1 to 4. Job strain = mean demands / mean control. Demands and control also converted to percentage scores (demands <math>\alpha=0.65</math>, control <math>\alpha=0.81</math>)</i>
Negative affect (NA) over a working day and evening*	NA = angry or irritated, sad or upset, anxious or worried <i>Emotions scored 1-5 at 5 timed intervals over a working day and evening, mean score range 1-5 (<math>\alpha=0.82</math>)</i>
Anxiety, HADS-A	Anxiety: 'I feel tense or 'wound up', 'Worrying thoughts go through my mind'. <i>Rated on a frequency scale 0 to 3, range 0-21 (<math>\alpha=0.81</math>)</i>
Depression, HADS-D	Depressive symptoms: 'I still enjoy the things I used to enjoy', 'I have lost interest in my appearance'. <i>Rated on a frequency scale 0 to 3, range 0-21 (<math>\alpha=0.76</math>)</i>
Sleep problems, Jenkins Sleep Scale*	How often in the past four weeks did you: 'Have trouble falling asleep?', 'Wake up after your usual amount sleep feeling tired and worn out?'. <i>Scored on a 6-point scale from 1 'not at all' to 6 '21 to 31 nights per month', scaled out of 100 (<math>\alpha=0.74</math>)</i>
Social support at work*	Do you agree or disagree with the following statements: 'I have a good relationship with my manager(s)', 'I am getting on well with my colleagues'. <i>Responses on a 4-point scale from 1 'strongly disagree' to 4 'strongly agree', higher scores indicating more support, mean score 1-4 (<math>\alpha=0.72</math>)</i>
Mindfulness, Freiburg Mindfulness Inventory (FMI)	Thinking about the last two weeks.. 'I see my mistakes and difficulties without judging them'; 'I pay attention to what's behind my actions'. <i>Responses were given along a 4-point scale from '1' rarely to '4' almost always, range 14-56 (<math>\alpha=0.86</math>)</i>
Secondary biological outcomes (assessed at T1 and T2 only)	
Blood pressure*	Self-assessed at 5 intervals over the working day and evening using a wrist monitor. Two readings were taken at each time point. Mean BP was based on an average of all readings over the day.
Hair cortisol concentration*	Determined from a 2cm segment proximal from the scalp. Steroid extraction and immunoassay conducted at Dresden Technical University.
Process measures	
Meditation time	1. Objective progress, based on download data 2. Self-reported progress through the programme (final day completed)
App feedback	Reasons for not using the app, any changes noticed since starting the programme, suggestions to improve the app, intention to re-use the app, whether would recommend to a friend
Background measures	
Demographics	Age, sex, work seniority, part-time/full-time, weekly work hours over the last month
Health behaviours	Smoking, exercise frequency
Self efficacy	Confidence will listen to the app most days, confidence the app will be effective

\*Assessed at T1 and T2 only

As discussed previously (sections 2.2.3, 7.5.3), hair from the posterior scalp may provide a month-by-month calendar of cortisol levels (Kirschbaum et al., 2009). Observational studies suggest hair cortisol demonstrates strong test-retest reliability ( $r=0.68$  to  $0.79$ ) over three months and one year later. Hair strands of a diameter of 2-3mm were cut from the scalp from a posterior vertex position. Hair samples were placed in foil, indicated with the direction of the scalp end, labelled with participant ID, and placed in a plastic bag for transportation and storage. Cortisol concentrations were determined from the 2cm hair segment most proximal to the scalp. Based on an average hair growth rate of 1 cm/month (Wennig, 2000), this segment represents hair grown over the two month period prior to hair sampling. Wash and steroid extraction procedures were carried out at the Technical University, Dresden, according to a previously described protocol (Kirschbaum et al., 2009).

Following extraction, cortisol levels in both studies were determined using a commercially available immunoassay with chemiluminescence detection (CLIA, IBL-Hamburg, Germany). The intraassay and interassay coefficients of variation of this assay are below 8%. Two samples were taken from 10% participants to assess reliability. Participants also completed a brief hair questionnaire to assess frequency of hair washing with shampoo (Hamel et al., 2011) and recent dye or chemical treatment since these factors may influence cortisol concentration (Stalder and Kirschbaum, 2012) (Appendix 8.ix). In order to ensure that groups were matched for BMI in blood pressure and cortisol analyses, baseline height and weight were measured at baseline ( $BMI = \text{weight (kg)} / \text{height (m)}^2$ ).

#### *Process measures*

Meditation practice was measured objectively via data from the app, which recorded the number of days of the programme which had been completed. Participants who had downloaded the app were asked whether had experienced any changes as a result of the programme, good or bad (open question); if they intended to continue using the app after the trial (yes/no); whether they would recommend it to a friend who was feeling stressed (yes/no).

#### *Background measures*

Background measures were included to check the characteristics of the sample and as potential factors influencing meditation time. Measures included baseline age, sex, full-

time/part-time work, estimated working hours over the last month (<37/38-45/46-54/55+ hours, assessed at T1, T2 and T3). Health behaviours were smoking (current/non-smoker) and exercise frequency (days per week typically complete 30 minutes physical exercise).

### **Statistical analysis**

Data from both sites were combined in the primary analysis. Baseline values were compared between experimental groups (app versus wait-list control) using t-tests for normally distributed continuous data and chi-squared tests for categorical data. Bivariate Pearson correlation coefficients ( $r$ ) were calculated to explore baseline correlates of well-being. Hair cortisol concentration and negative affect were positively skewed and were log transformed to improve the fit to a normal distribution. BMI was categorised as underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) or obese (30+). Only four participants were underweight so the first two categories were combined. Age ranged from 23-24 to 60-61 in both settings, but 50% of participants were aged 30-40. To improve fit to a normal distribution age was divided into quintiles as a covariate in linear models. Post-intervention outcomes were analysed on an intention-to-treat (ITT) basis with missing values at T2 replaced by the baseline value (last observed response carried forward) (Twisk and de Vente, 2002). In sensitivity analyses, hypotheses 1, 2 and 3 were re-tested based on complete cases.

*Hypotheses 1 & 2:* A series of separate 2 x 2 repeated measures ANCOVAs with time (T1/T2) as the within-subjects factor and treatment group (app/wait-list) as the between-subjects factor were used to identify significant group by time interactions. Site (A/B) and change in average work hours (increase/no change/decrease from T1 to T2) were included as covariates in repeated measures ANCOVAs to account for contextual differences. Analyses of biological outcomes also co-varied for age, sex and BMI. Hair washing frequency with shampoo (daily/less) and colour hair treatment within the last two months (yes/no) were included as covariates in cortisol analyses (Hamel et al., 2011). The effect of the intervention was considered significant if there was an interaction between group and time ( $p < 0.05$ ) and change scores (T2-T1) were in the hypothesised direction. Partial eta-squared ( $\eta^2$ ) was used as a measure of effect size which can be interpreted similarly to Cohen's criteria for small (0.01), medium (0.06) and large (0.14) effect sizes (Cohen, 1969). Differences in change scores between groups were compared with independent t-tests. Where significant site by

time interactions indicated statistically significant differences in outcomes by site over time, separate analyses were conducted within each site to test whether results effects of the intervention generalised across sites.

*Hypothesis H3:* Objective meditation practice time had an irregular distribution. Correlations between practice time in the app group and outcome variables were first investigated using Spearman rank correlation coefficients (rs) for non-parametric data. Meditation practice was grouped into low (0-9 days/ $\leq 90$  min, n=41), medium (10-24 days/100-310 min, n=52) and high (25-45 days/ $\geq 310$  min, n=35) categories. These practice groups corresponded to not completing Take 10, completing Take 10 but not Take 15 and completing Take 15. Practice time was used as a grouping factor in a series of 2 (T1, T2) x 4 (wait-list/low/medium/high practice) repeated measures ANCOVAs to test effects of meditation practice time on outcomes. Change scores were calculated within each group to test the direction of hypothesised associations. Post-hoc tests with a Bonferroni correction were used to identify significant differences between groups.

*Longer term effects:* Exploratory analysis of the stability and reproducibility of intervention effects at T3 was based on responders to the online questionnaire only, in the absence of a control group. Twenty-two percent (n=52) participants did not respond at T3. Firstly, to see whether changes in the app group were maintained over 3 months, paired t-tests were used to assess differences between well-being at T2 versus T3 (app group only). Secondly, to see whether the intervention was associated with similar benefits in both groups, paired t-tests were used to assess differences between changes in well-being at T2 – T1 in the first app group versus T3 – T2 in the wait-list group.

*Hypothesis H4:* Analyses to test mechanisms linking meditation time with changes in outcomes over time were based on complete cases within the app group. Bivariate associations between meditation time, potential mediators (*changes in well-being, negative distress, mindfulness*) and outcomes (*changes in job strain, BP, cortisol*) were initially tested with Pearson correlation coefficients. Mindfulness was tested as a mediator because self-

reported mindfulness has been shown to mediate effects on stress reduction in previous studies (Nyklicek and Kuijpers, 2008; Baer et al., 2012). Mediation pathways were tested using PROCESS, a conditional process modelling program introduced in Chapter 5 (section 5.2) (Hayes, 2012). Potential mediators were initially tested in separate models linking meditation time (low/ medium/ high) indirectly with change in each outcome. Variables associated with significant indirect effects were then tested in a combined model using PROCESS model 4, which allows for up to 10 mediators. Covariates were baseline levels of the dependent variable and baseline mediator values, site and change in work hours. Age, sex and BMI were included as covariates for biological outcomes, plus hair colour and hair wash frequency for cortisol. All indirect effects were subjected to follow-up bootstrap analyses with 1,000 bootstrap samples and a 95% confidence interval. SPSS Version 21.0 was used for all analyses.

#### *Changes to planned protocol: cortisol assessed on complete cases basis*

At T1, n=57/238 participants were missing cortisol data (24%). Reasons included: hair too short to cut (<1cm, n=21), routine use of steroid medication (n=9), opted not to give a hair sample (n=27). At T2 a further n=29 opted not to give a sample and n=5 participants had hair too short (n=21 wait-list, n=13 app group). Participants with cortisol values more than 150pg/mg (n=6) or changes over time of more than 100% (n=4) were excluded from the analysis on the basis of possible external contamination (Thomson et al., 2010; Pereg et al., 2011). Therefore n=101 participants (42%) were missing cortisol data at T1 or T2. Cortisol analyses were based on n=137 participants with valid cortisol data at T1 and T2 (app group n=75, 59%; wait-list n=62, 56%).

### **8.3.3 Results**

#### *Participant recruitment and retention*

In total 341 employees completed the screening questionnaire, 266 of whom were eligible to participate (Figure 8.10). Most of those excluded were being treated for a relevant medical condition (n=40) or did not own a smartphone (n=19). Five reported no overcommitment and n=11 were only prepared to participate if they started in the app group. Invitations to participate were issued to 257 employees until 240 baseline interview slots were filled. Two participants withdrew on the day of interview and could not be re-scheduled, resulting in an

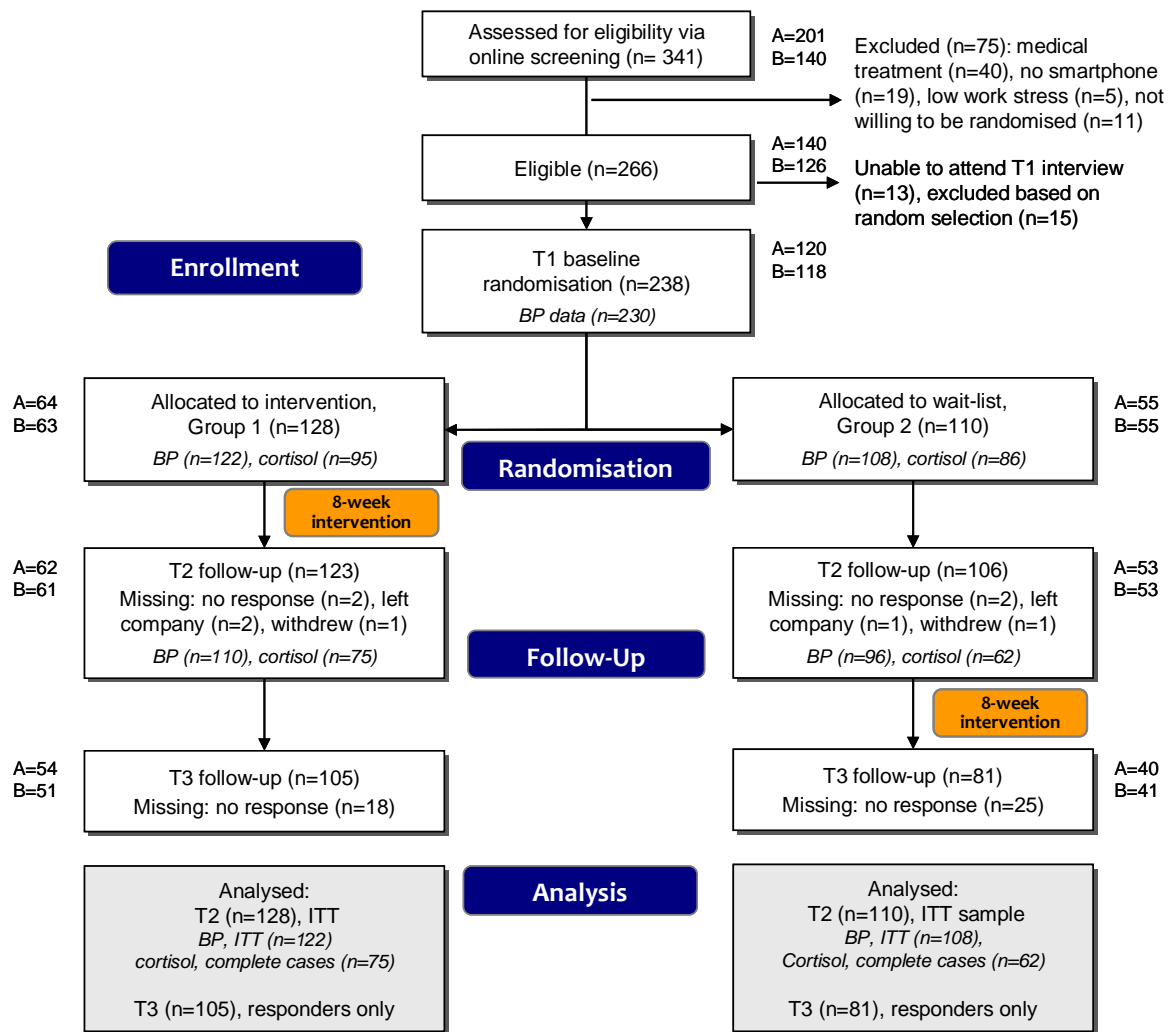


enrolled sample of n=238; 120 at Site A and 118 at Site B. All participants completed baseline psychological measures at an onsite interview and n=230 (97%) returned a completed BP and affect diary the following day.

A random number generator was used to allocate 55 participants per site to the control group (n=110) and remaining participants to the intervention (n=128). The optional launch event was attended by 52% of the app group (n=35 at Site A, n=32 at Site B). After the 8 weeks allocated for the intervention, there were no significant differences in retention by intervention group, by site or between groups within each site. T2 psychological measures were completed by 96% participants in both the app and wait-list groups (n=115 at Site A, n=114 at Site B). Similar numbers of participants were lost to follow-up within each group at each site (n=3 app group, n=2 wait-list at Site A; n=2 per group Site B). Complete BP diaries were returned by n=206 participants, equivalent to 90% of those who measured BP at T1 in both the app and wait-list groups (n=106 at Site A, n=102 at Site B). Reasons for missing BP data were: n=9 left the study, n=9 unable to attend an interview but completed online measures, n=7 failed to provide at least 3 BP readings at the same time intervals over the day at both T1 and T2. Online questionnaires at T3 were completed by 82% participants in the first app group and 75% participants in the wait-list group (n=95 Site A, n=91 Site B).

At Site A, recruitment started on 28<sup>th</sup> February 2012. T1 interviews were completed from 19<sup>th</sup> March to 3<sup>rd</sup> April. The intervention launched on 18<sup>th</sup> April, after Easter. T2 interviews were completed between 11<sup>th</sup> and 28<sup>th</sup> June and participants completed T3 questionnaires online over two weeks from 22<sup>nd</sup> August. At Site B, recruitment started on 6<sup>th</sup> August. T1 interviews took place from 26<sup>th</sup> August to 6<sup>th</sup> September and the intervention launched on 7<sup>th</sup> September. T2 measures were completed from 4<sup>th</sup> to 22<sup>nd</sup> November. The T3 online questionnaire was available for two weeks from 21<sup>st</sup> January. CONSORT diagrams for each site are included in Appendix 8.xi.

**Figure 8.10 Participant CONSORT flow diagram**




### *Baseline characteristics of intervention and control groups*

Baseline characteristics of participants are summarised in Table 8.5. There were no significant differences between app and control group participants either within site, or when both sites were combined.

**Table 8.5 Baseline characteristics of trial participants**

Mean scores (standard deviation), or percentages where indicated. Independent t-tests conducted to compare app vs. wait-list group and to compare Site A vs. Site B

		<b>App group</b>	<b>Wait-list group</b>	<i>Site A</i>	<i>Site B</i>
		<b>n=128</b>	<b>n=110</b>	<i>n=120</i>	<i>n=118</i>
Age		36.0 (8.3)	35.0 (6.9)	38.2 (7.9) <sup>^^</sup>	32.9 (6.4)
Seniority at work, 1-10		4.9 (2.1)	4.8 (1.8)	4.8 (2.1)	4.9 (1.8)
Female, %		60.2	58.2	68.3 <sup>^</sup>	50.0
Work hours >45/week, %		45.3	47.3	33.3	59.3 <sup>^^</sup>
Work part-time, %		3.1	4.5	5.0	2.5
Well-being (WEMWBS)		47.4 (6.8)	46.8 (5.9)	46.5 (6.9)	47.8 (5.7)
Positive affect, work day*		3.2 (0.5)	3.2 (0.5)	3.2 (0.5)	3.2 (0.5)
Job strain, ratio		1.08 (0.21)	1.07 (0.24)	1.10 (0.21)	1.06 (0.23)
Demands		81.9 (12.1)	80.9 (11.8)	81.4 (11.5)	81.5 (12.5)
Control		76.7 (9.1)	77.1 (11.1)	75.2 (10.2)	78.6 (9.7) <sup>^^</sup>
Social support		3.2 (0.5)	3.2 (0.5)	3.2 (0.5)	3.2 (0.5)
Depression (HADS-D)		5.0 (3.4)	5.1 (3.2)	5.4 (3.6)	4.8 (2.9)
Anxiety (HADS-A)		9.2 (3.9)	9.3 (4.0)	9.5 (3.9)	9.0 (4.0)
Negative affect, work day*		1.8 (0.6)	1.9 (0.6)	1.8 (0.6)	1.9 (0.6)
Sleep problems		3.0 (1.3)	3.1 (1.1)	3.0 (1.3)	3.0 (1.1)
Mindfulness (FMI)		33.4 (7.4)	33.7 (6.9)	33.3 (7.6)	33.8 (6.8)
Systolic BP, mmHg*		111.3 (10.0)	111.3 (11.0)	112.2 (10.6)	110.3 (10.2)
Diastolic BP, mmHg*		69.5 (7.3)	69.9 (8.3)	70.2 (7.5)	69.1 (8.0)
Hair cortisol, pg/mg log <sup>\$</sup>		3.06 (0.56)	3.08 (0.56)	2.79 (0.39)	3.35 (0.56) <sup>^^</sup>
Will listen daily (5/5), %		45.3	52.7	57.5 <sup>^^</sup>	39.8
Will be effective (4+/5), %		48.4	50.0	50.0	48.3
Overweight (BMI 25+), %		44.1	37.6	48.7 <sup>^^</sup>	33.3
Current smoker, %		16.4	14.5	16.7	14.4
Exercise >2/week. %		44.5	45.5	36.7	53.4 <sup>^</sup>

\*based on n=122 app group, 108 wait-list group; <sup>\$</sup> based on n=75 app group, n=62 wait-list group

<sup>^^</sup>Site A vs Site B t-test  $p \leq 0.01$ , <sup>^</sup> $p < 0.05$

Well-being in trial participants was slightly lower than the national average reported in Health Survey England, an annual population survey (mean 51.5 for employees in England)(Bryson et al., 2011). Levels of anxiety were also higher than expected within a general population sample: n=166 (70%) trial participants scored  $\geq 8$  on the HADS anxiety scale and n=50 (21%) for HADS depressive symptoms, compared with 28.8% and 18.5% respectively in a large Norwegian population sample (Olsson et al., 2005). Compared with the airline pilots studied in Chapter 5, trial participants at both sites reported higher levels of demands (>80% vs. 71.4%  $\pm$  12.6) but also higher levels of control (>75% vs. 58.8%  $\pm$  8.2)

resulting in overall lower job strain ( $<1.10$  vs.  $1.23 \pm 0.31$ ). Baseline levels of mindfulness were similar across sites but lower than levels reported in a sample of over 500 French workers (mean FMI  $39.0 \pm 5.4$ )(Trousselard et al., 2010).

The majority of participants had blood pressure within a healthy range: 82.3% had systolic readings  $<120$ mmHg and 89.2% reported diastolic pressure  $<80$ mmHg. Only four participants started with systolic readings  $>140$  mmHg and three had a diastolic pressure  $>90$ mmHg. There were no significant differences in baseline characteristics between those that provided valid blood pressure data at T1 and T2 and those that did not, either within each site, or combined. Similarly, those who provided hair samples for cortisol analysis ( $n=137$ ) did not differ significantly from those without. When the sample was restricted to those with cortisol data at T1 and T2, there were no significant differences between baseline characteristics of the intervention group compared with the control group for any of the variables listed in Table 8.5.

#### *Differences in baseline characteristics by site*

The range of ages was similar across sites (Site A 24-60 years; Site B 23-61 years) but 43% of participants at Site A were aged  $\leq 35$  years compared with 73% at Site B. Two thirds of Site A participants were female, which was representative of the wider office population. Site A participants were more likely to be overweight and less likely to exercise regularly than participants at Site B. Mean hair cortisol concentration was lower at Site A but there were no between site differences in blood pressure. Site B participants reported higher mean job control, but longer estimated working hours, with 12% working more than 55 hours per week over the previous month compared with 0.8% at Site A. Overall levels of well-being and job strain were similar at both sites.

Most participants were confident that they would be able to find 10-20 minutes per day to meditate but self-efficacy was higher at Site A: on a scale of 1 to 5, where 5 was 'very confident', mean scores were  $4.5 \pm 0.6$  at Site A and  $4.2 \pm 0.8$  at Site B. Participants were less confident that listening to meditation podcasts would make them feel different about work: mean scores out of 5 were  $3.5 \pm 0.9$  at both sites.

### *Baseline (T1) correlates of well-being and outcomes*

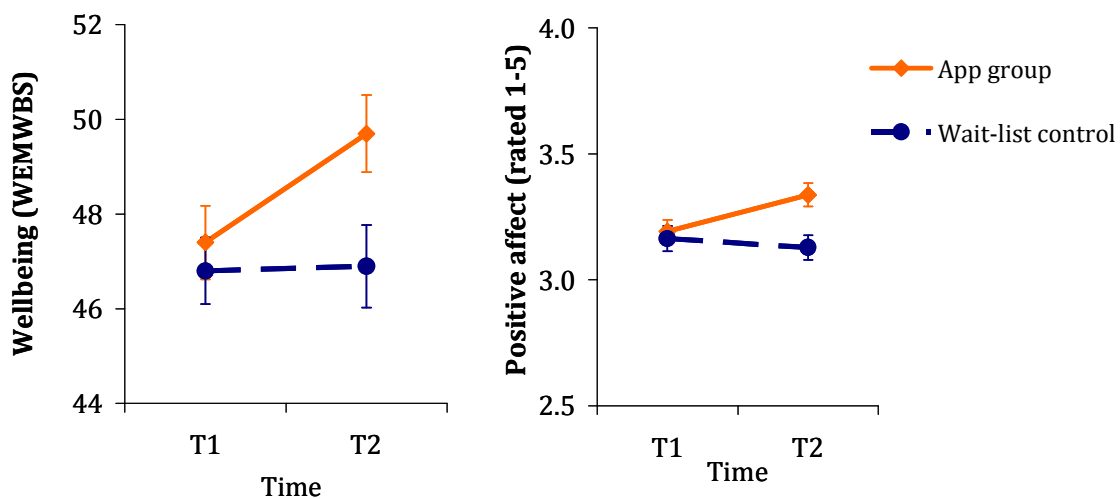
At baseline, both well-being (WEMWBS) and experienced positive affect over the day were inversely correlated with job strain ( $r = -0.34$ ,  $r = -0.29$ ;  $p < 0.001$ ) and positively correlated with mindfulness ( $r = 0.56$ ,  $r = 0.31$ ;  $p < 0.001$ ). Mindfulness was inversely correlated with job strain ( $r = -0.32$ ,  $p < 0.001$ ). Depression, anxiety and negative affect over the day each had a positive correlation with job strain ( $r = 0.29$ ,  $r = 0.38$ ,  $r = 0.34$  respectively; all  $p < 0.001$ ) and a negative association with mindfulness ( $r = -0.44$ ,  $r = -0.48$ ,  $r = -0.370$ ; all  $p < 0.001$ ). Neither blood pressure nor cortisol was correlated with psychological well-being, negative distress or job strain at T1.

### **Hypothesis 1: Increases in well-being will be higher in the app group**

In repeated measures ANCOVAs, there were significant group by time interactions for WEMWBS well-being ( $F(1,234) = 9.67$ ,  $p = 0.002$ ) and positive affect over the day ( $F(1,226) = 7.90$ ,  $p = 0.005$ ). Increases in both subjective well-being indicators were larger in the app group than the wait-list control group, as illustrated in Figure 8.11 and described in Table 8.6. The effect size for both outcomes was small to moderate. There were no significant interactions between experimental group and study site or change in work hours in these effects. The first hypothesis under investigation was therefore confirmed, since participants randomised to the app condition did show larger improvements in well-being.

**Figure 8.11** Changes in primary outcomes, WEMWBS well-being and positive affect over the day from baseline (T1) to post-intervention (T2)

Participants randomised to the app group and wait-list control groups. Mean scores  $\pm$  standard error.



**Table 8.6 F statistics for repeated measures ANCOVAs intervention group by time interactions and effect sizes**  
Change scores (T2-T1) are listed to illustrate the direction of changes over time in each experimental condition

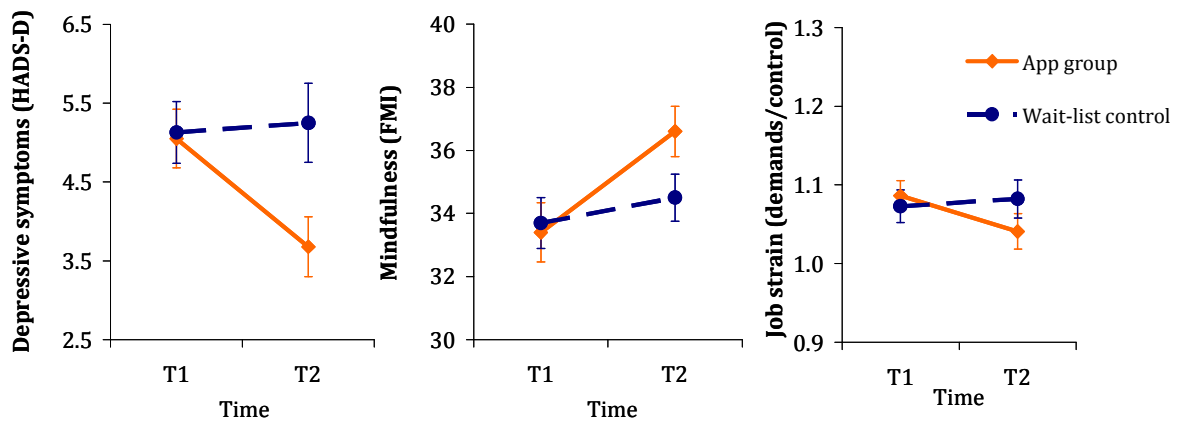
Outcomes	All participants		Change scores Post intervention - Pre intervention	
	Group*time interaction F (1,234)	$\eta_p^2$	App group (n=128)	Wait-list group (n=110)
Well-being, WEMWBS	<b>9.67**</b>	0.040	2.3 (5.6)	0.06 (5.7)
Positive affect <sup>a</sup>	<b>7.90**</b>	0.034	0.15 (0.46)	-0.03 (0.52)
Job strain	<b>5.95*</b>	0.025	-0.04 (0.17)	0.01 (0.18)
Demands	1.65	0.007	-1.2 (9.9)	0.28 (11.2)
Control	<b>5.18*</b>	0.022	2.2 (6.3)	0.23 (6.0)
Social support	<b>4.84*</b>	0.020	0.12 (0.52)	-0.01 (0.41)
Depression, HADS	<b>17.7**</b>	0.070	-1.4 (2.9)	0.13 (2.9)
Anxiety, HADS	<b>8.87**</b>	0.037	-1.6 (3.3)	-0.47 (3.0)
Negative affect <sup>a</sup>	<b>6.91**</b>	0.030	-0.05 (0.57)	0.13 (0.57)
Sleep problems	<b>4.46*</b>	0.019	-0.33 (4.5)	-0.06 (0.81)
Mindfulness, FMI	<b>12.0**</b>	0.049	3.2 (5.9)	0.76 (4.8)
Systolic BP, mmHg <sup>a</sup>	<b>4.50*</b>	0.020	-0.39 (4.5)	0.77 (4.1)
Diastolic BP, mmHg <sup>a</sup>	2.27	0.010	-0.21 (3.4)	0.31 (3.0)
Cortisol, pg/mg log <sup>b</sup>	0.004	<0.001	-0.14 (0.38)	-0.13 (0.41)

<sup>a</sup> n=230, <sup>b</sup> n=137 Repeated measures ANOVAs adjusted for site and change in work hours. \*\*p<0.01, \*p<0.05. BP analyses additionally adjusted for age, sex and bmi. Cortisol adjusted for hair dye and washing frequency.

## **Hypothesis 2: Allocation to the app group will be associated with appropriate changes in secondary outcomes versus the wait-list control group**

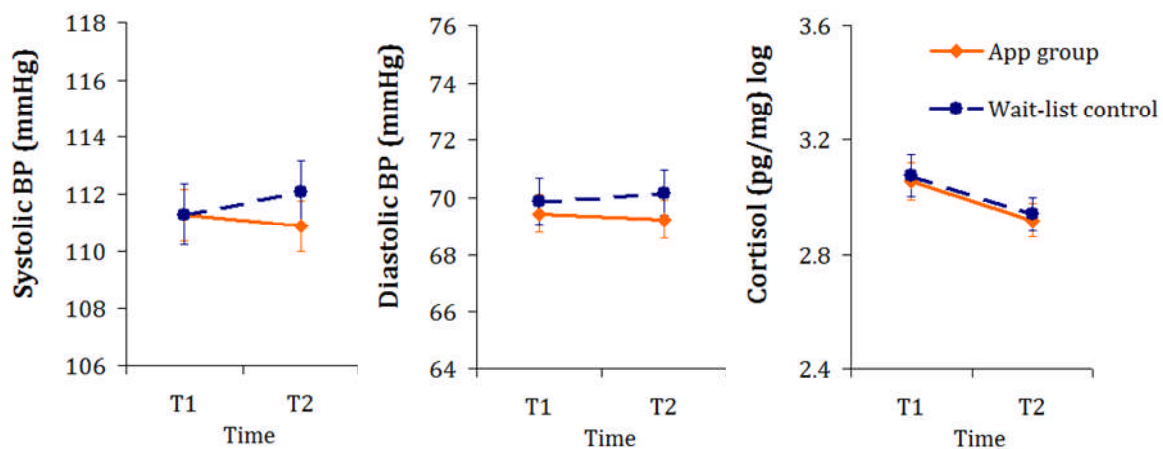
As listed in Table 8.6, there were significant experimental group by time interactions with change scores in the hypothesised directions for (in order of decreasing effect size): decreased depressive symptoms (*moderate-sized effect*), increased mindfulness, decreased anxiety, decreased negative affect over the day, decreased job strain and decreased systolic BP (*small effect size*). Changes over time for depressive symptoms, mindfulness and job strain are illustrated in Figure 8.12. In addition, the app group reported decreased sleep problems and increased social support relative to the wait-list group.

**Figure 8.12 Changes in depressive symptoms, mindfulness and job strain from baseline (T1) to post-intervention (T2)**  
Participants randomised to the app group and wait-list control groups. Mean scores  $\pm$  standard error.



From T1 to T2 there was a small uplift in systolic BP in the wait-list group and a small decrease in the app group, resulting in an overall significant group by time interaction  $F(1,223)=4.50$ ,  $p=0.035$ . A similar trend occurred for diastolic BP, but the group by time interaction was not statistically significant ( $p=0.134$ ). Hair cortisol concentration decreased to a similar extent over time in both experimental groups, with no evidence of a group by time interaction (Figure 8.13).

**Figure 8.13 Changes in blood pressure and cortisol from T1 to T2**  
Participants randomised to the app group and wait-list control groups. Mean scores  $\pm$  standard error.

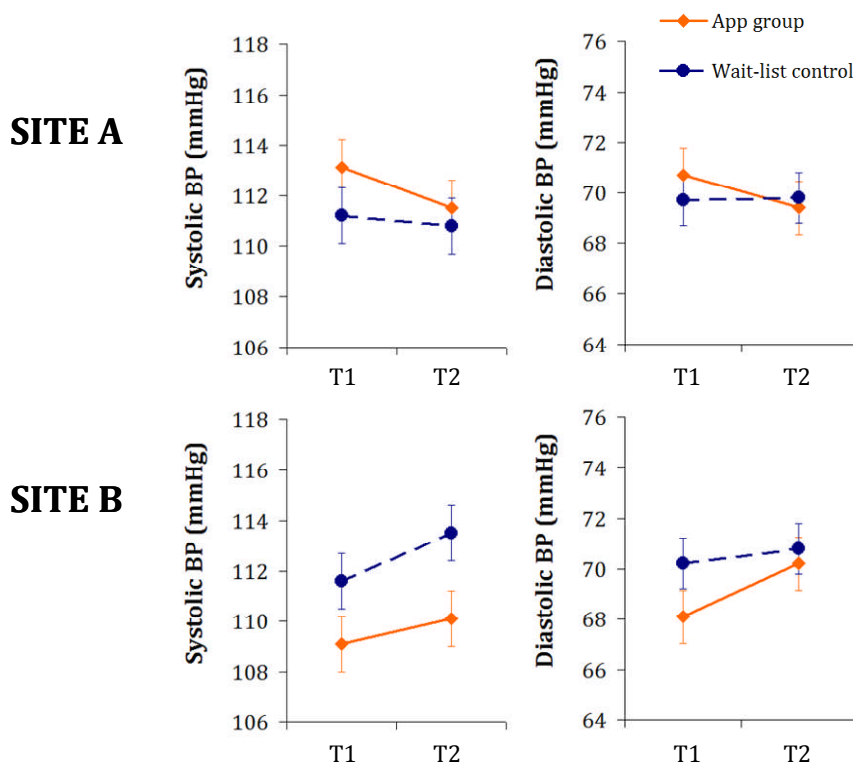


### *Differences in intervention effects by site: blood pressure*

Site was entered as a covariate into ANCOVAs to confirm the consistency of effects. The only significant time by site interactions were for systolic and diastolic BP,  $F(1,223)=15.85$  systolic, 15.17 diastolic (both  $p<0.001$ ), after adjusting for age, sex, BMI and change in work hours. The patterns of change in BP over time at each site are illustrated in Figure 8.14. There was an unexpected trend for BP to increase at Site B in both the app and wait-list groups. When ANCOVAs were repeated within each site, there was a significant group by time interaction for diastolic BP at Site A ( $p=0.010$ ) with the hypothesised decrease in the app group, but no significant effect on diastolic BP at Site B ( $p=0.716$ ). Group by time effects on systolic BP did not reach significance within either site, but the effect at Site A was in the hypothesised direction. It is unclear why BP changes varied by site. The mean number of BP readings recorded, out of 5, was similar: Site A  $4.7 \pm 0.6$ ; Site B  $4.5 \pm 0.8$ . When comparisons were restricted to those who measured BP at all 5 time intervals over the day ( $n=133$ ), site by time interactions remained significant (systolic BP  $p=0.048$ , diastolic BP  $p=0.003$ ) and BP showed the same pattern of decreasing over time at Site A and increasing at Site B. There were no significant changes in exercise or smoking behaviour at either site during the trial, either within or between experimental groups.

**Figure 8.14** Change in blood pressure from T1 to T2 at Site A and Site B

Participants randomised to the app group and wait-list control groups. Unadjusted mean scores  $\pm$  standard error.





**Table 8.7 Self-reported average weekly working hours over the last month**  
Work hours at each site at baseline (T1) and post-intervention (T2)

	Site A	Site B	Site A vs B	Combined	Combined
	%	%	<i>Chi-squared</i>	App group	Wait-list group
				%	%
T1 >45 hrs/week	33.3	59.3	p<0.001	45.3	47.3
T2 >45 hrs/week	27.0	65.8	p<0.001	45.6	50.5
Hours decreased during trial	20.5	19.7		16.0	14.0
Hours stayed the same	74.8	59.8		68.8	65.4
Hours increased during trial	14.8	20.5	*p=0.043	15.2	20.6

Estimated work hours were more likely to increase at Site B than Site A during the trial (Table 8.7) but change in this variable did not explain the site by time interaction for BP. There were no differences in psychological outcomes by site (Appendix 8.xii). There was a weak correlation between change in work hours and change in job demands ( $r_s=0.15$ ,  $p=0.021$ ), but no significant association with change in control or job strain. Change in work hours was retained as a covariate in all analyses combining both sites, to control for contextual differences in work demands over time.

In sensitivity analyses based on complete cases, the sample size for psychological outcomes was reduced from  $n=238$  to  $n=229$ . For BP and affect over the day the sample size was  $n=208$  (ITT=230). All significant experimental group by time interactions reported in Table 8.6 remained significant with the exception of the treatment effect on systolic BP, ( $F(1,201)=2.04$ ,  $p=0.155$ ). The treatment group by time interaction association with diastolic blood pressure approached significance ( $F(1,201)=3.16$ ,  $p=0.077$ ).

These findings indicate only partial support for hypothesis 2; as hypothesised, participants randomised to the app condition showed larger increases in mindfulness and reductions in job strain and measures of negative distress. There was a trend for reduced BP in the app group relative to the wait-list group, but effects were not consistent across sites and a significant effect based identified in ITT analyses was not robust in complete cases analysis, suggesting a false positive. There were no intervention effects on hair cortisol concentration.

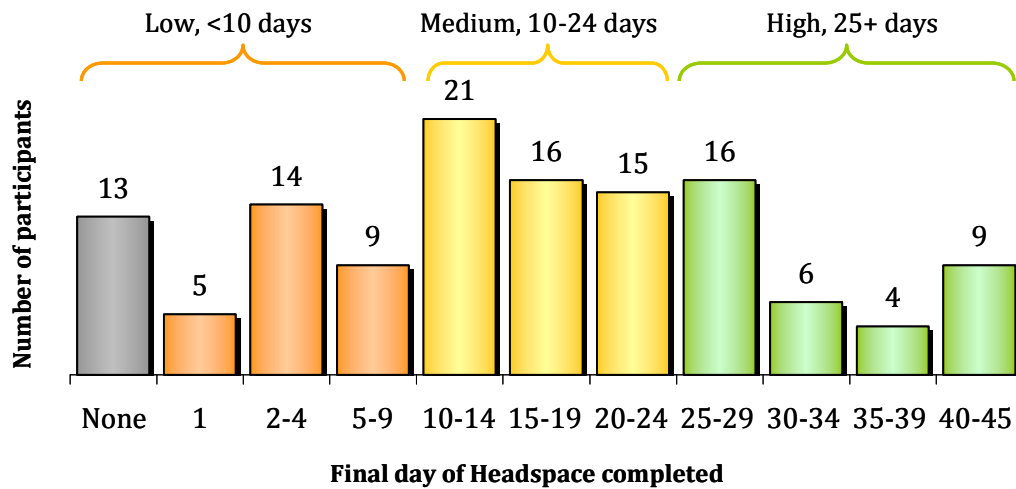
### Hypothesis 3: Longer meditation practice time will predict stronger effects

App group participants completed an average  $16.6 \pm 12.9$  days of the Headspace programme (range 0-45 days), equivalent to  $222 \pm 201$  minutes meditation (range 0-725 min) over 8 weeks from T1 to T2 (Table 8.8, Figure 8.15). Thirteen participants did not use the app;  $n=3$  cited technical reasons and  $n=10$  lack of time. Overall 74% participants completed more than 6 days (60 min), 68% completed 10 days or more (100+ min), 27% completed 25 days or more (325+ min) and 2% completed all 45 sessions (725 min). Meditation practice was not correlated with baseline psychological or demographic characteristics, working hours or change in working hours. Site A participants completed on average three more days of the programme than Site B, but the difference between sites was not statistically significant ( $p=0.195$ ). Participants' confidence that they would find time to meditate, or that meditation would be effective, were not correlated with practice time. Attendees of the introductory talk (52%) completed on average 5.9 more days meditation than non-attendees (19.9 vs. 14.0 days,  $p=0.010$ ). Anticipated meditation effectiveness did not differ between attendees and non-attendees before the talk (both groups  $3.5 \pm 0.9$  out of 5).

**Table 8.8** Progress through the Headspace programme, based on download data

<i>App group only</i>	App group % (n=128)	Site A % (n=65)	Site B % (n=63)
Meditation practice			
Mean days completed (SD)	16.6 (12.9)	18.1 (13.0)	15.1 (12.6)
Mean meditation time, min (SD)	222 (201)	244 (201)	199 (201)
Did not use the app	13	9	4
Completed 1-9 days only	28	9	19
10-24 days (completed Take 10)	52	24	28
25+ days (completed Take 15)	35	23	12

**Figure 8.15 Number of participants who completed each stage of the Headspace programme**  
Based on download data from the app, divided into meditation practice time groups



#### *Association between meditation practice time and outcomes*

Within the app group, meditation practice time was correlated with increases in well-being (WEMWBS) ( $r_s = 0.25$ ,  $p = 0.005$ ) and positive affect over the day ( $r_s = 0.23$ ,  $p = 0.011$ ) and with decreases in HADS depressive symptoms ( $r_s = -0.25$ ,  $p = 0.003$ ) and anxiety ( $r_s = -0.36$ ,  $p < 0.001$ ). Practice time was not significantly correlated with changes in negative affect ( $r_s = -0.06$ ) or job strain ( $r_s = -0.04$ ). Meditation practice was categorised into low (0-9 days/ $\leq 90$  min/Take 10 incomplete,  $n = 41$ ), medium (10-24 days/100-310 min/Take 15 incomplete,  $n = 52$ ) and high (25-45 days/ $\geq 325$  min/completed Take 15,  $n = 35$ ) groups.

In 2 x 4 repeated measures ANCOVA with time as the within-subjects factor and meditation practice group (low/medium/high plus wait-list) as the between-subjects factor, adjusted for site and working hours, there were significant practice group by time interactions for well-being, positive and negative affect over the day, anxiety, depression and mindfulness but no significant associations with biological outcomes (Table 8.9).

Longer meditation practice time was associated with a large negative effect on anxiety (HADS-A,  $\eta_p^2 = 0.116$ ) and depressive symptoms (HADS-D,  $\eta_p^2 = 0.097$ ) and moderate positive effects on mindfulness ( $\eta_p^2 = 0.073$ ), well-being (WEMWBS,  $\eta_p^2 = 0.066$ ) and positive affect over the day ( $\eta_p^2 = 0.059$ ; all  $p < 0.01$ ). Well-being increased by +4.1, +2.3 and +0.6 ( $\pm < 5.9$ ) in the high, medium and low practice groups respectively, compared with +0.06 in the wait-list

group. Longer practice time was associated with a small effect on negative affect ( $\eta_p^2=0.041$ ;  $p=0.024$ ) but there was not a linear association between meditation time and change in negative affect. Figure 8.16 illustrates the changes over time for the outcomes which had significant meditation group by time interactions; there were no significant baseline differences.

**Table 8.9 Association between meditation practice group and outcomes**  
F statistic for group by time interactions based on separate repeated measures ANCOVAs

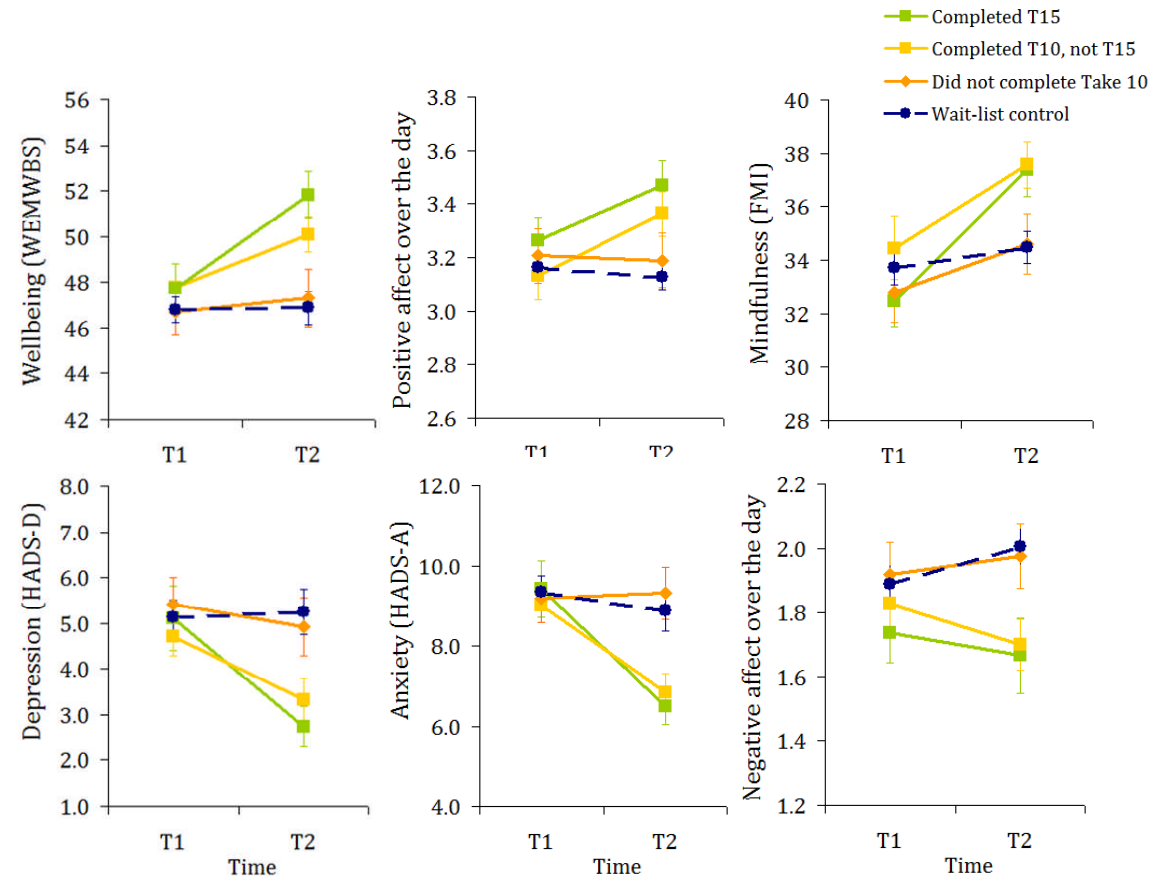
Outcomes	Repeated measures ANCOVA, meditation practice group*time interaction		Change scores T2-T1 within each meditation practice time group		
	F (1,232)	$\eta_p^2$	Low, did not complete T10	Medium, completed T10 not T15	High, completed T15
Well-being, WEMWBS	<b>5.50**</b>	0.066	0.6 (5.9)	2.3 (5.8)	4.1 (4.5) <sup>c,l</sup>
Positive affect <sup>a</sup>	<b>4.67**</b>	0.059	-0.02 (0.4)	0.2 (0.5) <sup>c</sup>	0.2 (0.4)
Job strain	2.24	0.028	-0.02 (0.2)	-0.05 (0.2)	-0.07 (0.2)
Demands	0.79	0.010	0.00 (11.2)	-1.0 (9.3)	-2.9 (9.3)
Control	2.16	0.027	1.3 (4.9)	2.8 (7.0)	2.2 (6.8)
Social support	1.73	0.022	0.09 (0.5)	0.1 (0.6)	0.1 (0.5)
Depression, HADS	<b>8.31**</b>	0.097	-0.5 (3.1)	-1.4 (2.8) <sup>c</sup>	-2.4 (2.4) <sup>c,l</sup>
Anxiety, HADS	<b>10.10**</b>	0.116	0.1 (3.1)	-2.2 (2.8) <sup>c,l</sup>	-2.9 (3.2) <sup>c,l</sup>
Negative affect <sup>a</sup>	<b>3.22*</b>	0.041	0.06 (0.5)	-0.1 (0.5)	-0.07 (0.7)
Sleep problems	2.00	0.025	-0.4 (0.9)	-0.2 (1.2)	-0.5 (1.0)
Mindfulness, FMI	<b>5.81**</b>	0.073	1.8 (4.7)	3.1 (5.6)	4.9 (7.3) <sup>c</sup>
Systolic BP, mmHg <sup>a</sup>	2.40	0.032	-0.2 (3.7)	0.3 (5.2)	-1.6 (4.2) <sup>c</sup>
Diastolic BP, mmHg <sup>a</sup>	2.27	0.010	0.3 (2.7)	-0.7 (4.1)	-0.08 (3.2)
Cortisol, pg/mg log <sup>b</sup>	0.24	0.006	-0.09 (0.4)	-0.2 (0.4)	-0.1 (0.3)

<sup>a</sup>  $n=231$ , <sup>b</sup>  $n=137$  Repeated measures ANOVAs adjusted for site and change in work hours. \*\* $p<0.01$ , \* $p<0.05$ . BP analyses additionally adjusted for age, sex and bmi. Cortisol adjusted for hair dye and washing frequency. Post hoc analyses with Bonferroni correction: <sup>c</sup> significant difference from wait-list group; <sup>l</sup> significant difference from low practice time group

Post hoc tests showed that participants completing Take 15 (325+ min) demonstrated significantly larger changes over time than the wait-list group for well-being, depression, anxiety, mindfulness and systolic BP. There were no differences in outcomes between wait-list participants and those in the low practice group. There were no statistically significant differences in change scores for those in the medium versus high practice time groups, but

there was a trend for the high group (completed Take 15) to show greater improvements in psychological health (Figure 8.16).

**Figure 8.16 Well-being, positive affect, mindfulness, depression, anxiety and negative affect by meditation practice group**  
Mean scores  $\pm$  standard error



Site by time interactions were significant only for systolic and diastolic BP, driven by the overall trend for increased in BP at Site B and decreased BP at Site A (discussed above). Change in BP was not significantly associated with meditation time within either site, but there was a trend for those in the highest practice group to show a reduction in systolic BP (not diastolic BP) at both sites (Appendix 8.xiii).

In sensitivity analyses based on complete cases, all the significant interaction effects highlighted in Table 8.9 remained statistically significant.

These results support the hypothesised association between meditation practice and greater increases in WEMWBS well-being and positive affect over the day. Longer practice

was also associated with larger effects on mindfulness, depression and anxiety but did not have a linear association with changes in job strain, BP or cortisol.

#### *App feedback*

Of those who downloaded the app, 84% agreed that they would recommend it to a friend and 84% intended to continue using it after the first eight week trial. Feedback to open questions about the experience of using the app was positive and very similar to feedback from pilot participants; qualitative results are therefore discussed in more detail in Appendix 8.xv.

#### *Outcomes at T3, 8 weeks after the wait-list group accessed the app*

Wait-list participants were offered the intervention after T2 interviews. The app group were told that they had completed the trial but were still able to access the app. A short questionnaire was completed online by 186 participants (78%) on average 10 weeks later. Between T2 and T3, the first app group reported a small uplift in anxiety,  $0.62 \pm 3.1$ , but all other psychological outcomes remained stable. Changes in well-being and job strain for wait-list respondents from T2 to T3 were similar in magnitude to app respondents from T1 to T2. These results are discussed in more detail in Appendix 8.xiv.

### **Hypothesis 4: Changes in well-being will mediate intervention effects on job strain and biological outcomes in the app group, independent of negative distress**

#### *Bivariate correlations*

Analyses to investigate the mechanisms of change over time in the app group were based on participants with complete data at T1 and T2. Table 8.10 lists correlations between meditation time and changes in well-being, mindfulness, job strain, BP and cortisol in the app group. In support of hypothesis 4, meditation time was positively correlated with changes in well-being and positive affect over the day but not directly associated with job strain or biological outcomes. Changes in WEMWBS well-being and positive affect over the day had an inverse correlation with change in job strain, as did changes in mindfulness. Counter to hypothesis 4, changes in BP and cortisol were not significantly correlated with changes in well-being or negative distress but there was a trend for changes in positive and negative affect over the day to have opposite associations with change in blood pressure.

**Table 8.10 Correlations between changes in all positive and negative psychological indicators, mindfulness, job strain and biological outcomes**  
Based on complete cases within the app group from T1 to T2

	$\Delta$ Well-being	$\Delta$ PA <sup>a</sup>	$\Delta$ FMI	$\Delta$ Job strain	$\Delta$ NA <sup>a</sup>	$\Delta$ HADS-D	$\Delta$ HADS-A
<i>Meditation time</i> <sup>\$</sup>	<b>.208*</b>	<b>.228*</b>	.155	-.043	-.062	<b>-.246**</b>	<b>-.359**</b>
$\Delta$ Well-being	-	<b>.248*</b>	<b>.424**</b>	<b>-.178*</b>	<b>-.305**</b>	<b>-.584**</b>	<b>-.430**</b>
$\Delta$ PA over day <sup>a</sup>	<b>.261*</b>	-	.161	<b>-.207*</b>	<b>-.403**</b>	<b>-.223*</b>	<b>-.275*</b>
$\Delta$ Mindfulness	<b>.425**</b>	.163	-	<b>-.231*</b>	<b>-.187*</b>	<b>-.355**</b>	<b>-.407**</b>
$\Delta$ Job strain	<b>-.178*</b>	<b>-.196*</b>	<b>-.202*</b>	-	<b>.209*</b>	.138	<b>.360**</b>
$\Delta$ Systolic BP <sup>a</sup>	.004	-.049	.045	-.020	.160	.162	.169
$\Delta$ Diastolic Bp <sup>a</sup>	.043	-.163	.100	.048	.133	.094	.120
$\Delta$ Cortisol (log) <sup>b</sup>	.109	-.180	.108	.003	-.122	-.081	-.126

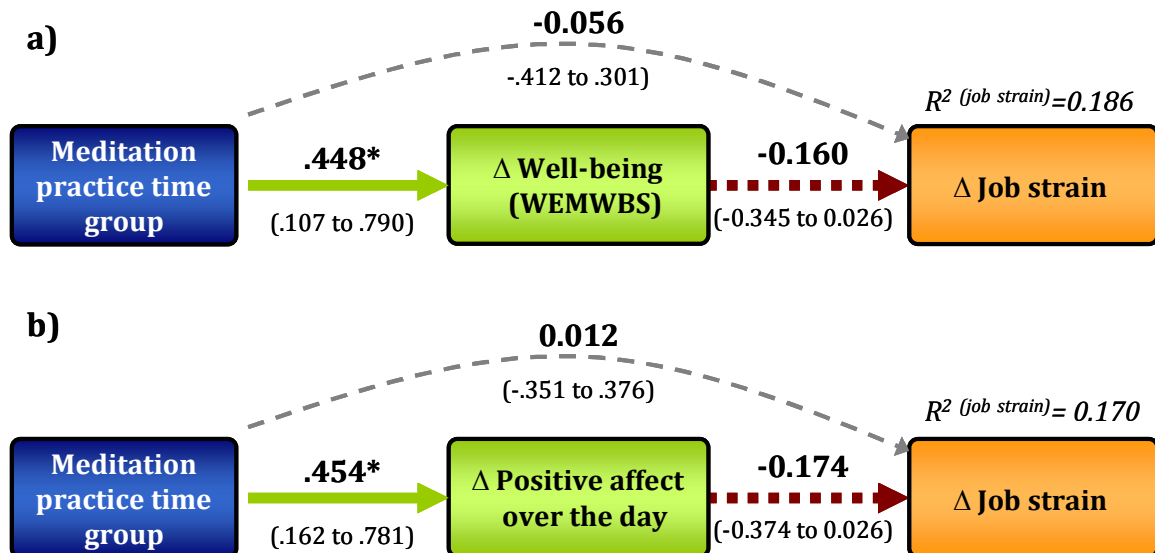
\*\*p≤0.001, \*p≤0.05. Pearson correlation coefficients, change scores T1 to T2. \$Spearman's rank coefficients. <sup>a</sup>n=110 <sup>b</sup>n=75. FMI=Freiburg Mindfulness Inventory; HADS=Hospital Anxiety and Depression Scale

Interestingly in the wait-list group, although the magnitude of changes over time was smaller (Table 8.6), changes in job strain was still significantly correlated with WEMWBS well-being ( $r = -0.211$ ,  $p = 0.030$ ) and less so with positive affect ( $r = -0.40$ ,  $p = 0.162$ ) and mindfulness ( $r = -0.173$ ,  $p = 0.078$ ). There was a trend for changes in well-being and positive affect to have inverse correlations with changes in diastolic BP ( $r = -0.122$ ,  $-0.132$ ; both  $p > 0.175$ ) and a significant association between changes in well-being and systolic BP ( $r = -0.227$ ,  $p = 0.021$ ).

#### *Indirect effects from meditation practice to job strain in the app group*

Separate mediation models were created in PROCESS to test indirect pathways from meditation practice time to change in job strain via change in WEMWBS well-being or positive affect. In support of hypothesis 4, there were indirect effects of meditation practice time on job strain mediated by changes in well-being (indirect effect size  $-0.07$ , 95% C.I.  $-0.21$  to  $-0.01$ ) or positive affect (indirect effect size  $-0.08$ ; C.I.  $-0.24$  to  $-0.01$ ) (Figure 8.17). Indirect effects were significant despite there being only borderline significant regression coefficients from each well-being measure to change job strain in the adjusted models (well-being  $p = 0.09$ ; positive affect  $p = 0.09$ ). Associations between well-being and job strain were driven by an association with increased job control, rather than decreased demands. There was an indirect effect of well-being on change in job control as the dependent variable (indirect effect size  $-0.10$ ; C.I.  $-0.27$  to  $-0.01$ ) but no significant effect on job demands ( $-0.04$ ; C.I.  $-0.18$  to  $0.02$ ).

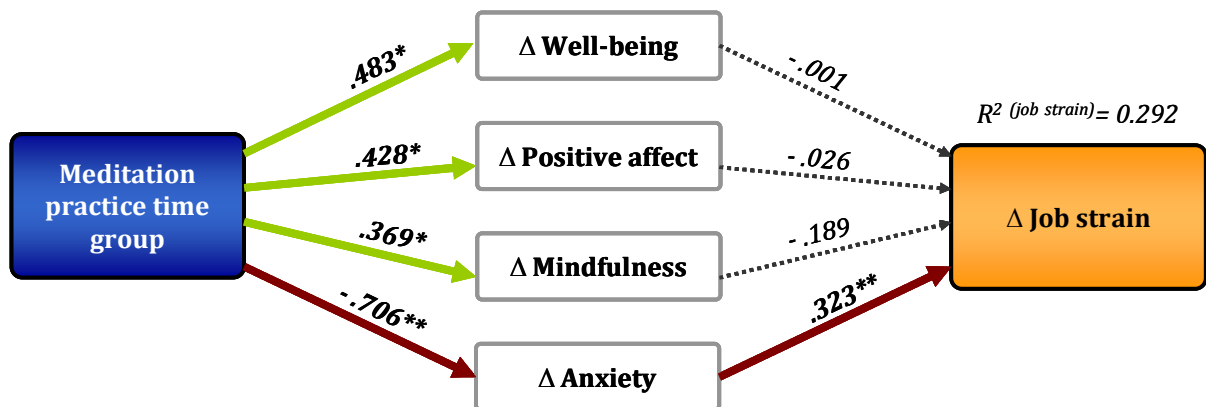
**Figure 8.17** Change in i) WEMWBS well-being ii) positive affect over the day as mediators of the association between meditation practice and change in job strain  
Regression coefficients calculated using PROCESS. Covariates were T1 job strain, T1 well-being/positive affect, site and change in work hours. \*\* $p \leq 0.001$ , \* $p \leq 0.05$ .



In separate models, there were also indirect effects from meditation practice to job strain via change in mindfulness (indirect effect size -0.10; C.I. -0.26 to -0.02,  $\Delta$ job strain  $R^2=0.218$ ) and a larger indirect effect via change in anxiety (-0.32; C.I. -0.54 to -0.16,  $\Delta$ job strain  $R^2=0.265$ ). There were no indirect effects on job strain via change in negative affect or HADS depression. Meditation time did not have a direct effect on change in job strain in any model. When well-being, positive affect, anxiety and mindfulness were tested as mediators in the same model, meditation time had a significant independent association with all four mediators but only the indirect pathway to job strain via change in anxiety was statistically significant (Figure 8.18). The  $R^2$  for the model was 0.292; a slightly better model fit than the model for change in anxiety alone.



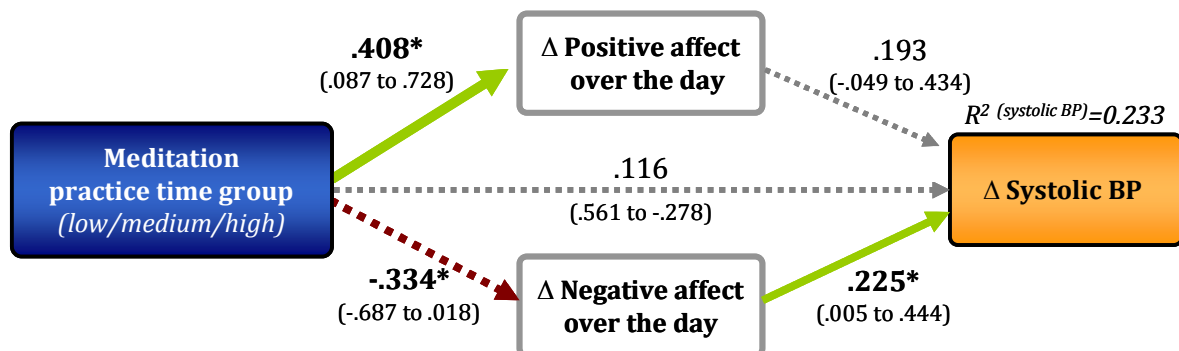
**Figure 8.18** Change in well-being, positive affect, mindfulness and anxiety as mediators of the association between meditation practice time and change in job strain  
Covariates were T1 job strain, well-being, positive affect, mindfulness anxiety, site and change in work hours. \*\* $p \leq 0.001$ , \* $p \leq 0.05$ .



#### Indirect effects from meditation practice to blood pressure and cortisol

Counter to hypothesis H4 there were no indirect effects of meditation practice on blood pressure or cortisol via WEMWBS well-being or positive affect over the day. Similarly changes in mindfulness, HADS depressive symptoms or anxiety were not associated with changes in biological outcomes after adjustment for covariates. Change in negative affect over the day had a significant indirect effect on systolic BP, an effect that was statistically significant of change in positive affect over the day (adjusted for site, change in work hours, age, sex and BMI). The indirect effect for negative affect was  $-0.08$  (95% C.I.  $-0.25$  to  $-0.01$ ) (Figure 8.19).

**Figure 8.19** Change in positive and negative affect over the day as mediators of the association between meditation time and change in systolic blood pressure  
Covariates were T1 systolic BP, positive affect, negative affect, site, change in work hours, age, sex and BMI. \*\* $p \leq 0.001$ , \* $p \leq 0.05$ .



Overall there was some evidence to support hypothesis 4. An indirect pathway from meditation time to changes in job strain via changes in subjective well-being measures was confirmed, but this association was not independent of changes in anxiety, or mindfulness. Changes in subjective well-being were not associated with changes in blood pressure or cortisol but change in negative affect did partially mediate an association with change in systolic blood pressure.

#### **8.3.4 Conclusions**

The significance of the trial findings relating to the effects of the mindfulness meditation app will be discussed first. The implications of this trial for the broader aims of the PhD, in relation to developing an understanding of the mechanisms linking positive well-being, job strain and biological processes, will be continued in the final discussion.

##### *Summary of intervention effects*

Employees randomly allocated to use a self-guided mindfulness meditation app reported significant increases in psychological well-being and positive affect over the day after 8-weeks compared with a wait-list group. The intervention was also associated with significant decreases in job strain, anxiety, depressive symptoms, negative affect over the day and sleep problems and increased mindfulness. There was a small reduction in systolic blood pressure in the app group relative to the wait-list group in the primary analyses, but this effect was not robust in sensitivity analyses. Participants who used the app for longer reported stronger improvements on mood and mindfulness. Reduced anxiety appeared to mediate an association between meditation practice time and decreased job strain. Psychological outcomes remained broadly stable 10 weeks after the initial follow-up.

##### *An app as a viable and effective mindfulness intervention*

This trial demonstrated for the first time that mindfulness meditation training delivered via a self-guided smartphone app was associated with significant improvements to psychological health. This reinforces findings from other studies which have reported benefits from mindfulness training outside the traditional group face-to-face delivery model, for example using practitioner-led online training (Wolever et al., 2012), self-driven web-based training

(Gluck and Maercker, 2011; Ljótsson et al., 2011; Krusche et al., 2012) or self-driven printed guidance (Hulsheger et al., 2012).

The app group showed small to moderate increases in well-being (WEMWBS) and EMA ratings of positive affect compared with the wait-list group. The effect size was comparable to a meta-analysis of mindfulness meditation studies which identified small positive effects on positive emotions (six studies) and well-being (17 studies) (Sedlmeier et al., 2012). In a meta-analysis of 11 wait-list controlled trials of standard mindfulness-based therapies (MBSR and MBCT), Hofmann et al. (2010) reported small-to-moderate effect sizes for depression and anxiety, and a moderate effect on depressive symptoms for healthy subjects (Hedge's  $g=0.51$ ). We similarly found moderate and small-to-moderate effect on depressive symptoms ( $\eta_p^2=0.070$ ) and anxiety ( $\eta_p^2=0.037$ ) from the HADS, suggesting that the short-term effectiveness of the Headspace app over 8-10 weeks was comparable to group-based mindfulness therapy for reduction of depressive symptoms in an initially healthy sample. Compared with group-based therapies, the app is low cost (currently retails at £3.74 per month), easily scalable, convenient for users, requires a lower time commitment than standard MBSR and consists of standardised content. The programme is not overseen by a therapist so may be unsuitable for some clinical populations.

#### *Longer meditation time was associated with specific outcome effects*

Only participants who completed 100 minutes or more of the mindfulness programme reported significant improvements in mindfulness and mood variables relative to the wait-list control group. This finding suggests that meditation practice caused improvements in well-being but since participants were not randomised to meditate for different amounts of time, it is possible that other factors (such as personality) explained both progress through the programme and changes in mood over time. Previous studies which have relied on self-reported practice diaries have reported inconsistent associations between meditation practice and study outcomes (Nyklicek and Kuijpers, 2008; Carmody and Baer, 2009). It is possible that participants could have downloaded and played days of the programme without actively listening, or without managing to attain a mindful state, but download data may still be a more accurate record of practice time than self-report diaries. Meditation practice time was not predicted by baseline demographic or psychological variables. Participants who attended an introductory launch event completed on average 6 more sessions than those who

did not attend. The event did not include any information that was not available on the app, but it is possible that orientation by an experienced mindfulness practitioner enhanced motivation to meditate.

#### *Mechanisms linking mindfulness meditation practice and job strain*

To my knowledge this is the first mindfulness trial to report a significant intervention effect on job strain, based on the Demand-Control model. Several randomised controlled trials of adapted MBSR programmes for the workplace have reported significant effects on general perceived stress (Shapiro et al., 2005; Klatt et al., 2009; Geary and Rosenthal, 2011; Wolever et al., 2012) but null group effects have also been reported (Jha et al., 2010; Malarkey et al., 2013). The Headspace app contained no explicit references to dealing with stress at work but still resulted in reduced perceptions of job strain, even after adjusting for changes in work hours. Mediation analyses suggested that decreased anxiety was the primary mediator of effects on job strain. Increased mindfulness and improved subjective well-being had weaker effects in separate models. Changes in these mediating variables were significantly correlated with one other and were measured at the same time so in practice these indirect effects are likely to overlap. The HADS anxiety scale contains one positively worded item (*'I can sit at ease and feel relaxed'*), blurring the distinction between positive and negative psychological pathways. It could be that changes in mindfulness pre-empted changes in anxiety or positive well-being (Carmody et al., 2009). Further trials with repeated outcome assessments during the intervention, for example each week, could test this theory.

Mindfulness meditation is thought to promote an emotional detachment or 'de-centring' from stressful scenarios (Holzel, 2011). This may result in dissociation from anxiety-provoking thoughts and may enable participants to view the work environment more objectively. Garland et al. (2011) described mindful emotion regulation as 'positive reappraisal', in which stressful events are re-interpreted as beneficial or benign, which would be consistent with the results in this trial. The reduction in anxiety might also signal a reduction in rumination, or prolonged negative thoughts about work; previous studies have found an inverse association between mindfulness and rumination (Raes and Williams, 2010). Reduced rumination would be consistent with the increase in positive affect and decrease in negative affect over the day. The intervention was associated with improved perceptions of job control, or one's sense of autonomy at work, but not with job demands. The broaden-and-

build theory suggests that positive emotions broaden mindsets and behaviours, leading to cycles of positive experiences which build psychological resources such as autonomy (Fredrickson, 2001) (see also section 1.2.2).

The final model with multiple mediators accounted for a substantial 29% of the variation in changes to job strain within the app group. Other potential pathways linking mindfulness meditation and work stress that were not tested in this study include improvements in empathy (Krasner et al., 2009) and cognitive function, such as working memory (Jha et al., 2010) and attention (Zeidan et al., 2010), which might influence performance and perceptions of job control. It is also likely that external work factors influenced changes in job strain; there were no deliberate manipulations of the work environment but demands of individual roles are likely to have changed over time. I adjusted for an estimate of change in work hours but did not assess other metrics of work intensity.

#### *Influences of the intervention on blood pressure*

Mindfulness meditation has previously been shown to be associated with clinically significant reductions in blood pressure but significant effects have been restricted to those who started with elevated baseline levels of blood pressure (McCraty et al., 2003; Goldstein et al., 2012). The intervention effects on systolic blood pressure in the current trial were small and were only statistically significant in the primary ITT analyses, not complete cases analyses. Nevertheless the trend for reduced systolic and diastolic BP in a normotensive population is promising and suggests that further studies in pre-hypertensive or hypertensive populations are warranted.

Unexpectedly, changes in average blood pressure at Site B increased, which was not related to the intervention, change in work hours or psychological variables. Site A readings were taken in March and June and Site B readings were taken in August and November. Seasonal decreases in temperature from T1 to T2 at Site B might have influenced blood pressure increases (Sharma et al., 1990). Alternatively it may be that five manual blood pressure readings over a single work day were insufficient to give a reliable measure of blood pressure. Assessment of blood pressure via 24-hour ambulatory monitoring, preferably on multiple days, would be a more reliable method to assess changes over time (Hodgkinson et al., 2011).

Counter to hypothesis 4, only changes in negative affect, not positive affect, were significantly associated with changes in blood pressure over the day within the app group after adjusting for baseline levels (systolic BP only). Inverse correlations between blood pressure and positive affect over the day were stronger than for WEMWBS, a recollected measure of well-being, as suggested in Chapter 3. The literature review in chapter 2.2.2 suggested that evidence linking negative affect and raised ambulatory blood pressure was more consistent than evidence for an opposite association with positive affect. Changes in blood pressure during the trial were small in magnitude so the study may have been under-powered to detect independent dynamic associations between positive and negative psychological factors.

#### *Influences of the intervention on hair cortisol*

The intervention was not associated with changes in hair cortisol concentration. Chronic stress exposure has been associated with high hair cortisol in several studies, though no studies to date have tested an association with job strain (Staufenbiel et al., 2013). There were no cross-sectional associations between psychological measures and hair cortisol at baseline. Cortisol decreased to a similar extent in both intervention groups and across both study sites but changes were not correlated with baseline or dynamic changes in psychological measures. No psychological trials have reported pre-post changes in hair cortisol concentration as an outcome so there are currently no suitable benchmarks against which to compare these results. One possible explanation for the null finding is that the post-intervention hair samples were taken too early to detect intervention-driven effects. Hair samples are thought to represent systemic cortisol integrated over the past two months, so the T2 sample measured cortisol output right from weeks 1 to 8 of the intervention (Stalder and Kirschbaum, 2012). Stronger effects on psychological outcomes were observed in participants who practiced for longer so it would have been preferable to test hair cortisol at T3, or at least four weeks post T2, to allow more time for physiological changes to occur.

Recent mindfulness trials have found no pre-post effects on changes in salivary cortisol despite improvements in subjective measures of stress (Klatt et al., 2009; Malarkey et al., 2013), including one intensive three month meditation retreat (Jacobs et al., 2013). The study by Jacobs and colleagues did report a correlation between higher trait mindfulness and lower afternoon and evening cortisol at baseline and follow-up. Longer term follow-up and

larger population sizes may be necessary to rule out an association between mindfulness training and cortisol.

### *Strengths and limitations*

The strengths of this study included the novel use of a mindfulness app which captured meditation practice time objectively, random assignment to intervention or control groups, low rates of attrition, repetition of the trial at two sites, assessment of outcomes based on validated psychological questionnaires, EMA ratings of affect and objective biological outcomes. Limitations included the use of an inactive wait-list control group, rather than an active comparison group. It is possible that observer effects may account for the differences in outcomes between experimental groups, but stronger effects associated with longer meditation duration do support the argument for causality. An appropriate control condition would ideally be structurally equivalent, in terms of the number and duration of sessions, and include a plausible therapeutic rationale (Baskin et al., 2003). I was unable to identify a suitable alternative to the Headspace app. A health education programme (HEP) designed to be structurally equivalent to the group-based MBSR programme without references to mindfulness has recently been validated as an active control intervention for MBSR (MacCoon et al., 2012). In a randomised controlled trial, both interventions were associated with psychological benefits, but only MBSR resulted in smaller post-stress inflammatory responses (Rosenkranz et al., 2013). The HEP may provide a blueprint for a future online or app active control conditions.

A serious limitation, particularly for assessment of biological outcomes, was the limited follow-up time. Biological outcomes were assessed only directly post-intervention owing to preferences of the employers and the constraints of a PhD timetable. Longer term follow-up assessments at multiple time-points would be preferable to investigate the mechanisms of change and the sustainability of impacts on psychological and biological outcomes. For practical reasons neither participants nor the researcher were blind to treatment group but psychological questionnaires were completed individually online to avoid interviewer bias (Choi and Pak, 2005).

It is important to note that this trial was conducted within companies which take an active approach to the prevention of work stress and the promotion of employee well-being.

For example, both sites included an on-site gym and provided access to a confidential Employee Assistance Programme telephone line. All participants in the study owned smartphones, were well educated and reported high levels of baseline job control. These findings may not be applicable to other settings or patient populations.

In conclusion, this trial suggests that self-administered mindfulness training using a smartphone app can improve psychological well-being, reduce work-related stress and may decrease systolic blood pressure in healthy working adults after eight weeks. No effects on hair cortisol were observed but the reliability of this measure for assessing changes in systemic cortisol over time is not clear. The results suggest that further trials to test the effects of the self-guided mindfulness meditation app on psychological and biological outcomes over a longer time period versus an active treatment control are warranted.



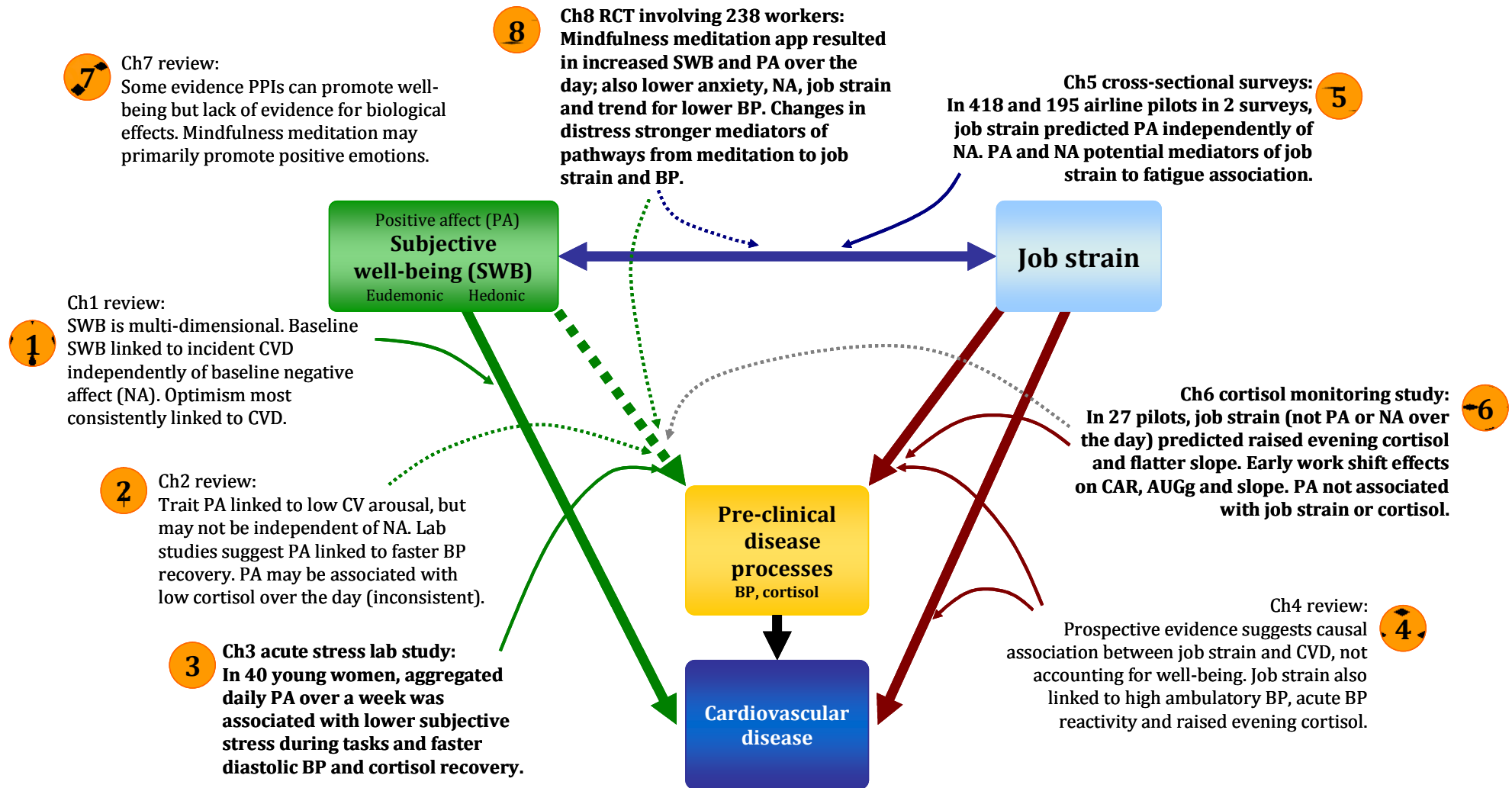
## Chapter 9 Discussion

The aim of this thesis was to investigate the mechanisms linking subjective well-being and cardiovascular disease. A review of prospective studies suggested that associations between well-being and cardiac outcomes were independent of baseline negative affect, but few studies had considered the role of chronic psychosocial stressors. Similarly, studies describing associations between positive affect and cardiovascular biomarkers rarely considered the role of chronic stress exposure. I examined job strain as an example of a chronic stressor with a likely causal effect on CVD. The relationships between indicators of well-being, negative affect, job strain, blood pressure and cortisol were explored using a variety of methods including systematic literature reviews, laboratory psychophysiological stress testing, cross-sectional surveys, a cortisol monitoring study and a randomised controlled trial. The key findings of each chapter are illustrated in Figure 9.1.

These studies highlight two-way interactions between well-being and job strain. Chapters 3 and 8 suggested that positive well-being influences appraisal of external stressors. Well-being and psychosocial stress may have independent (Chapter 3, Chapter 6) or overlapping opposite associations with biological markers (Chapter 8), depending on the measures. Chapter 5 suggested that both positive and negative affect could partially mediate the effects of job strain on health outcomes. Chapter 8 demonstrated for the first time that practicing mindfulness meditation using a smartphone app was associated with increased well-being and reduced job strain.

This discussion summarises the key findings, considers the overall contribution of the thesis to the literature and considers implications for research and practice. Limitations of the thesis and ideas for future research will be discussed.

**Figure 9.1 Summary of findings by chapter**  
(bold type highlights original empirical studies)



## **9.1 Summary of findings and contribution to the literature**

The question of whether subjective well-being has a causal (protective) effect on cardiovascular disease hinges on whether its effects are distinct from those of established psychosocial risk factors including chronic stressors such as job strain, mood disorders such as depression and anxiety and personality traits such as hostility. The relationship is further complicated by the multi-dimensional nature of subjective well-being. As outlined in Chapter 1, subjective well-being can be assessed using eudemonic measures, evaluative assessments such as life satisfaction and measures of hedonic experience. Well-being has a stable dispositional or trait aspect but positive and negative affective states also change in response to stimuli and over the day.

Evidence from ambulatory and laboratory studies reviewed in Chapter 2 suggested that trait, not state, measures of positive affect were associated with lower cardiovascular arousal. Associations between positive affect and blood pressure tended to be in the opposite direction to negative affect and sometimes independent. There was a mixed pattern of associations for positive affect and cortisol. The majority of studies suggested that well-being, based on retrospective or repeated measures of experienced positive affect, was associated with lower mean salivary cortisol over the day. Some studies suggested that associations with the diurnal cortisol rhythm were not independent of negative affect or depression. Few studies considered whether well-being was associated with biological outcomes independently of job strain, despite evidence (reviewed in Chapter 4) that job strain is associated with raised ambulatory blood pressure, blood pressure reactivity in susceptible individuals and higher evening cortisol.

In this thesis, I conducted four empirical studies to investigate the relationship between well-being and acute or chronic psychosocial stress. Findings are summarised as they relate to three potential patterns of association between well-being, stress and CVD processes: i) subjective well-being influencing stressors appraisal; ii) independent effects of well-being and psychosocial stress on biological outcomes; iii) reduced positive affect as a downstream mediator of chronic stress.

*i) Subjective well-being influences appraisal of acute and chronic stressors*

Chapter 3 tested the association between a dispositional measure of positive affect and subjective, cardiovascular and cortisol responses to standardised mental stress tasks under controlled conditions in 40 young women. Higher positive emotional style (PES) derived from mean daily measures of positive mood over seven days was associated with lower subjective stress and greater perceived control during the tasks, regardless of task performance. PES also predicted faster blood pressure recovery, an association that was not explained by perceived stress, as discussed in point ii) below. This study reinforced findings from earlier studies in which positive affective dispositions predicted lower reported stress during acute mental tasks (Papousek et al., 2010; Endrighi et al., 2011). The advantage of the laboratory approach was that the environment was tightly controlled. All participants received the same instructions so differences in perceived stress were more likely attributable to individual characteristics than exposure. However, findings from the laboratory may not generalise to daily life. The study did not include a measure of chronic stress so it is possible that the measure of PES over seven days was influenced by un-measured stress exposures.

Boehm and Kubzansky (2012) hypothesised that positive psychological well-being could be associated with perceptions of stressors as challenges rather than threats, but the authors commented on the difficulty of understanding the dynamics between well-being and stress; does stress influence well-being or vice versa? Chapter 5 of this thesis identified an inverse association between job strain and recalled positive affect that was independent of negative affect but the cross-sectional methodology meant it was not possible to confirm the direction of associations. I identified only one previous study which had examined longitudinal associations between well-being and constructs from the demand-control model over time. In an observational study based on three time-points over four years, Armon et al. (2012) found evidence of reciprocal causal associations between vigour and job control independent of neuroticism. Vigour did not predict change in demands.

The randomised controlled trial in Chapter 8 was designed to test the hypothesis that increased well-being would alter perceptions of job strain without changing the external work environment. I used a mindfulness meditation app as an intervention to promote well-being. Within the intervention group, there was evidence to support the hypothesised pathway from

meditation practice time to reduced job strain via increased well-being. Changes in two measures of well-being, positive affect over the day and a combined eudemonic and hedonic measure, statistically mediated the changes in job strain. Associations were independent of changes in work hours. However, mediation effects were not specific to well-being; reduced anxiety appeared to have a stronger influence on job strain than well-being. This study demonstrated that there is an affective component to the appraisal of job strain, particularly job control. Changes in meditation time and psychological variables explained 30% of the variance in job strain over time.

*ii) Independent effects of well-being and psychosocial stress on biological processes*

In Chapter 3, regardless of perceived stress levels, PES predicted rapid diastolic blood pressure recovery. This study confirmed previously reported findings from our group and others that dispositional measures of positive affect are associated with rapid diastolic blood pressure recovery from stress in young adults, independently of negative affect (Steptoe et al., 2007a; Dowd et al., 2010; Papousek et al., 2010). Chapter 3 also showed for the first time that dispositional positive affect predicted a lower salivary cortisol response to acute stress, independent of depressive symptoms. A recalled measure of positive affect over the last few days predicted blood pressure recovery but not cortisol reactivity. Although these associations were limited to the laboratory, blood pressure recovery and cortisol reactivity in the lab have been linked to increased risks of hypertension (Stewart and France, 2001; Hamer and Steptoe, 2012) and coronary calcification (Hamer et al., 2012) indicating that dispositional positive affect might also be linked to lower risks of these outcomes.

Chapter 6 described a 6-day salivary cortisol monitoring study in 27 male pilots during early shifts, late shifts and rest days. Job strain was associated with raised evening cortisol and a flatter cortisol rhythm, a pattern consistent with previous research (Rystedt et al., 2008). This study had the advantage of ecological validity but the intensive nature of the sampling protocol meant sample size was restricted. Counter to the a priori hypothesis, positive affect based on happiness ratings at the time of saliva samples was not significantly associated with cortisol. It is possible that this study was under-powered to detect effects. Chronic job strain may result in a chronic inability to physically ‘unwind’ at the end of the day which is independent of affective states on the day. This could reflect impaired central negative feedback sensitivity of the HPA axis, as has been described in obesity (Mattsson et al.,

2009). Raised evening salivary cortisol and a high flat rhythm have been linked to increased risks of cardiovascular mortality (Kumari et al., 2011).

In Chapter 8, the meditation trial, there was a trend for changes in daily positive affect to be inversely correlated with changes in blood pressure after eight weeks. Change in well-being based on WEMWBS, a single retrospective measure of eudemonic and hedonic well-being, was not correlated with change in blood pressure. When changes in positive and negative affect were entered into the same model, only change in negative affect had a significant association with change in systolic blood pressure after eight weeks. Job strain was not associated with blood pressure in this study at baseline or over time. Ambulatory monitoring over multiple days and follow up over a longer time period would have offered a more reliable assessment of blood pressure effects.

### *iii) Reduced positive affect as a downstream mediator of chronic stress*

The studies in thesis provided only very limited support for this pathway. Evidence for a causal effect of job strain on depressive symptoms suggested that psychological well-being would decrease as consequence of chronic stress exposure (Stansfeld et al., 2008). In Chapter 5, analyses of two cross-sectional workforce surveys consisting of over 400 airline pilots suggested that positive and negative affect, based on retrospective measures over the last two weeks, were feasible mediators of the association between job strain and fatigue, and between job strain and sleep problems. However, all variables were measured at the same point in time so the direction of causality could not be confirmed. As noted above, positive affect over the day did not explain associations between job strain and evening cortisol in the small study in Chapter 6. Job strain was not associated with blood pressure changes in Chapter 8. These studies do not suggest that experienced affect over the day is a primary link between chronic job strain and blood pressure or salivary cortisol.

## **Implications**

The findings of this thesis are consistent with the broad theory that subjective well-being reflects an adaptive capability to respond to acute and chronic stressors, rather than simply the absence of stress (Rozanski and Kubzansky, 2005). Independent associations between positive and negative affect and a number of biological processes have been reviewed previously (Pressman and Cohen, 2005; Steptoe et al., 2009; Boehm and Kubzansky, 2012),

but this thesis highlights evidence for the role of dispositional positive affect in stressor appraisal, in addition to distinct effects on biological recovery to acute stress. The findings of this thesis are consistent with the idea that the protective effects of well-being are partly attributable to the appraisal of environmental stimuli as a controllable challenge rather than a threat (Lazarus, 1991). In the context of acute stress this may result in reduced activation of the neuroendocrine system and rapid recovery of the cardiovascular system, as observed in Chapter 3. In the context of a chronic stressful environment, a more positive outlook may lower perceptions of stress and result in lower levels of experienced negative affect, which may mean lower levels of activation of the autonomic nervous system and a lower chronic allostatic load than for less positive individuals under the same circumstances (Rozanski and Kubzansky, 2005). Cognitive pathways that were not explicitly explored in this thesis which may also contribute to an association between well-being and autonomic flexibility include positive perceptions of one's own coping resources (Folkman, 2008) and the avoidance of rumination or chronic worry (Brosschot et al., 2006). There has been some attention to the idea that negative affectivity may bias perceptions of job strain (Hintsanen et al., 2011) but the idea that positive affect may have an independent influence on self-reported measures of job strain has not yet been explored in prospective cohort studies. This thesis suggests that researchers should consider potentially independent influences of job strain, positive and negative affect on disease processes and CVD outcomes.

Chapters 3 and 8 showed that multiple ratings of experienced positive affect were more likely to be associated with biological correlates than single retrospective measures of positive affect or the composite WEMWBS. Monitoring studies reviewed in section 2.2.2 identified more reliable associations between cardiovascular activation and trait than state positive affect. These findings reinforce findings from previous studies which suggested that repeated measures of affective experience reflect positive dispositional traits to a greater extent than recalled measures, which are more vulnerable to memory-experience gaps (Pressman and Cohen, 2005; Steptoe et al., 2007a; Miron-Shatz et al., 2009). The assumption in this thesis, as explained in section 1.2.4, has been that repeated measures of positive affect, eudemonic and hedonic well-being all reflect the same underlying construct of subjective well-being. Repeated measures of positive affect may be more sensitive to intra-individual variation, which might be important in understanding relationships with health outcomes.

Further research is required to understand the extent to which measures of experienced positive affect over time reflect changes in eudemonic well-being and evaluative measures over time, and vice versa, to confirm that subjective well-being is a valid umbrella term. External ratings of dispositional affect by partners or colleagues could be investigated as an alternative to repeated measures of positive affect.

The findings of this thesis have implications for the design and delivery of stress management interventions, reviewed in section 7.4.1. Traditional stress management approaches which focus on identifying stress triggers and coping mechanisms could be broadened to include mindfulness meditation and/or PPI approaches to bolstering well-being. The study in Chapter 8 identified a mediating role for reduced anxiety symptoms in the reduction of job strain, suggesting that where CBT-approaches are already in place, positive psychology approaches should complement, not necessarily replace, approaches which target psychosocial distress at work. It is important to note that measured factors accounted for only 30% of the variance in change in job strain. Individual interventions which may influence perceptions of control at work should not be seen as an alternative to designing job roles with manageable time pressures, non-conflicting demands, management support and skill discretion. It has been estimated that the cost of CHD and mental disorders arising from job strain in France, which has a similar population size to the UK, is between 1.8 and 3 billion euros per year, which is over 0.1% of GDP (Sultan-Taieb et al., 2013). Over three quarters of these estimated costs were due to sickness absence resulting from mental disorders. There is a strong economic argument for widening access to interventions to prevent and alleviate job strain.

Chapter 8 demonstrated that mindfulness meditation training could be accessed flexibly at low cost by healthy employees using a smartphone application. These findings may also be relevant to improving access to mindfulness-based therapies for patients. A recent paper which investigated the implementation of mindfulness-based cognitive therapy (MBCT) within the NHS highlighted that nearly a decade since NICE recommended MBCT for recurrent depression, a minority of services have sufficient staff or budget to run MBCT classes (Crane and Kuyken, 2013). Trials with follow-up of more than a year's duration are still needed to assess longer term cost effectiveness of self-driven mindfulness training, compared with



group classes. There also remains a need to compare the mindfulness meditation app to other active interventions to confirm that benefits are specific to mindfulness. It may be that the Headspace programme, or a similar online or smartphone programme specially adapted for clinical populations, could help to relieve pressure on NHS services.

## **9.2 Limitations and ideas for further research**

Limitations of individual studies have been discussed at the end of each chapter. In this section I mention some of the over-arching limitations of the studies included within this thesis, and ideas to build on this research.

Firstly, in section 1.4 I presented a ‘dynamic’ model of well-being based on findings from the literature which illustrated the potential complexity of interactions between the three dimensions of well-being and individual characteristics such as personality, environmental factors such as the work environment, and lifestyle behaviours. Well-being is a dynamic construct, yet this thesis (and much of the reviewed literature), focuses on cross-sectional and short-term changes in positive affect in relation to a narrow range of stimuli. I focused only on interactions between job strain and well-being.

In order to gain a better understanding of the relationship between well-being and cardiovascular risk, there is a need for life-course analyses based on large population samples which will allow modelling of the trajectories of different dimensions of well-being in relation to both individual differences (personality, genetics) and external stressors (such as income, marriage, unemployment). For example, quantitative genetic modelling based on over 3,200 twin pairs from the Twins Early Development Study (TEDS) showed that depressive symptoms aged 12 were significantly heritable. There was some evidence of a gene-environment interaction with stronger genetic effects on depressive symptoms for children with a suboptimal family environment (Wilkinson et al., 2013). The TEDS study incorporates a range of questions to assess well-being. As the current teenagers from this cohort age, it will be possible to investigate genetic and environmental influences on well-being and to what extent these factors are independent of influences on depressive symptoms. It would also be interesting to explore to what extent genetic and environmental factors explain behavioural risk factors for CVD and the role of psychological well-being in these associations.

To understand the influence of well-being on hard cardiovascular outcomes it will be necessary to study older populations and more established cohorts. For example, the Whitehall study of over 10,000 civil servants was initiated in 1985. The first measures of well-being were introduced in phase three (1991-1994). To date two studies based on the Whitehall cohort have reported positive associations between baseline well-being measures and reduced risks of CVD (Boehm et al., 2011a; Boehm et al., 2011b), but patterns of changes in well-being over time have not yet been related to cardiovascular outcomes. Life satisfaction was repeated at phases five and seven, which could enable trajectories to be modelled in relation to behavioural and biological cardiovascular risk factors.

A second important limitation of this thesis is the focus on blood pressure and cortisol as biological outcomes. These biomarkers were selected owing to their widespread use in previous studies of job strain and well-being, prospective links to CVD and ease of measurement. As noted in section 2.2.4, well-being has been linked to a wider array of biological processes and markers implicated in CVD including inflammatory, immune and metabolic indices and telomere length. High frequency heart rate variability or vagal tone is a marker of cardiovascular risk which is thought to reflect autonomic flexibility (Thayer and Lane, 2007). While low HRV has been linked to depressive disorders, a number of small studies have shown that vagal tone is associated with higher dispositional positive affect (Oveis et al., 2009), social connectedness and self-regulatory capability (Kok and Fredrickson, 2010). Recent mindfulness-based interventions suggest that meditation may lead to increases in high frequency heart-rate variability, at least in the short term (Garland et al., 2010b; Krygier et al., 2013). Vagal tone may be a useful outcome for future intervention research as an objective indicator of well-being and future cardiovascular risk.

All the empirical studies within this thesis were based in relatively young, healthy individuals who were at low short-term risk of cardiovascular disease. The intervention study in Chapter 8 was limited to short-term follow-up. Although the trend for reduced blood pressure post-intervention and lower job strain at three months were promising, the findings of this trial alone have limited implications for public health.

I would like to test the effects of the Headspace app on well-being, psychological distress and cardiovascular biomarkers in a higher risk healthy population or within cardiac

patients. The most recent Cochrane review of psychosocial interventions for heart disease patients included 19 studies, most of which targeted stress, anxiety or depression, and found evidence for small to moderate reductions in depression and anxiety, but uncertain effects on cardiac outcomes (Whalley et al., 2011). A more comprehensive meta-analysis of 62 psychological intervention trials in CHD patients found only small effects on depressive symptoms overall, with CBT marginally showing the strongest effect (Dickens et al., 2013). Could mindfulness-based approaches, which may both increase well-being and lower perceptions of chronic stress, be more effective at preventing or slowing disease progression?

Randomised controlled trials comparing mindfulness-based therapies with usual care have reported reduced anxiety in patients with implantable cardioverter defibrillators (n=45)(Salmoirago-Blotcher et al., 2013) and lower psychological symptoms in outpatients with diabetes (n=139) (van Son et al., 2012). The need for individual contact with a practitioner, even by phone, limits the accessibility of these therapeutic approaches and increases the cost of clinical trials. It could be relatively simple to conduct a trial in which patients enrolled in cardiac rehabilitation were randomised to usual care, which typically includes exercise classes and brief health education (O'Driscoll et al., 2007), or usual care plus access to the Headspace programme. Most cardiac rehabilitation programmes already have established mechanisms for collecting individual clinical, psychological and behavioural data at baseline, 12-weeks and 12 months follow-up, which is collated by the National Audit of Cardiac Rehabilitation (NACR, 2012). According to the NACR, only 10% of UK cardiac rehabilitation programmes currently have access to a psychologist. If self-driven mindfulness training leads to incremental benefits for psychological and/or cardiovascular outcomes compared with usual care, access to the programme could be incorporated into cardiac rehabilitation pathways quickly and cheaply, offering a potentially cost effective public health intervention.

### **9.3 Concluding remarks**

This thesis set out to investigate the popular assumption that happiness has a protective effect against heart disease. In terms of the Bradford Hill criteria for causality, there is considerable evidence for a temporal association between well-being and incident disease. The findings are consistent with psychological well-being as a marker for healthy adaptability to acute and

chronic stressors, particularly in terms of favourable cognitive appraisals. There was some empirical evidence of a specific association between well-being and biological processes (independent of psychological distress), but this was limited to acute blood pressure and cortisol stress responses in the laboratory. Based on current evidence, it remains unclear whether psychological well-being has a unique and direct protective effect against cardiovascular disease. A workplace trial showed that well-being increased in the short term following self-guided mindfulness meditation practice in comparison to a wait-list condition, but effects on biological outcomes were inconclusive. Further longer term trials to examine effects of self-guided mindfulness training on psychological and biological outcomes versus active comparison interventions are warranted to determine whether such therapies could offer a novel contribution to cardiovascular disease prevention.

## Publications

**Bostock S**, Steptoe A. (2013) Self-guided mindfulness meditation using a smartphone application improves psychological well-being, job strain and blood pressure *Psychological Medicine* (under review)

Hamer M, **Bostock S**, Hackett R, Steptoe A (2013) Objectively assessed sedentary time and type 2 diabetes mellitus: a case control study *Diabetologia* (accepted for publication)

**Bostock S**, Steptoe A. (2012) Influences of early shift work on the diurnal cortisol rhythm, mood and sleep: within-subject variation in male airline pilots *Psychoneuroendocrinology* 38(4):533-41

**Bostock S**, Steptoe A. (2012) Association between low functional health literacy and mortality in older adults: longitudinal cohort study *BMJ* 344:e1602

**Bostock S**, Hamer M, Wawrzyniak A, Mitchell E, Steptoe A. (2011) Positive emotional style and subjective, cardiovascular and cortisol responses to acute laboratory stress *Psychoneuroendocrinology* 36; 1175—1183

Poole L, Steptoe S, Wawrzyniak A, **Bostock S**, Mitchell E, Hamer M. (2011) Associations of objectively measured physical activity with daily mood ratings and psychophysiological stress responses in women *Psychophysiology* 48; 1165–1172

## Conference presentations & posters

- |         |   |
|---------|---|
| Jun 13  | World Congress on Positive Psychology, Los Angeles USA<br>Paper: <i>Can an app boost well-being at work? A randomised controlled workplace trial to test a mindfulness meditation smartphone app</i>                              |
| Mar 13  | American Psychosomatic Society annual meeting, Miami USA<br>Young Scholar Award<br>Paper: <i>Can finding headspace reduce work stress? A randomised controlled workplace trial of a mindfulness meditation app</i>                |
| Dec 12  | UK Society for Behavioural Medicine, University of Manchester<br>Prize-winning presentation<br>Paper: <i>Work Stress? There's an app for that. A pilot randomised controlled trial of a mindfulness meditation smartphone app</i> |
| Nov 12  | Student Mental Health Matters Conference, Oxford University<br>Paper: <i>Celebrating good mental health; why happiness matters</i>  |
| Oct 12  | ELSA Wave 5 Launch Conference, Royal Society, London<br>Poster: <i>Low health literacy predicts mortality in older adults</i>   |
| Dec 11  | UK Society for Behavioural Medicine Conference, University of Stirling<br>Poster: <i>Low functional health literacy and mortality in England; a longitudinal study</i>  |
| Sept 11 | European Health Psychology Society Conference, Crete<br>Poster: <i>Fatigue in airline pilots; the importance of objective and psychosocial aspects of the work environment</i>  |

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## Appendix: Chapter 3

### 3.i) Summary of the laboratory session protocol

#### Measures

#### 3.ii) Positive emotional style

#### 3.iii) Mood and task ratings

#### 3.iv) Profile of Mood States, short form

### 3.i) Laboratory session summary protocol

- ❖ Review information sheet and complete consent form
- ❖ Confirm health status as in information sheet
- ❖ Check instructions were followed: medication / alcohol / exercise / smoking / caffeine
- ❖ Brief verbal explanation of session
- ❖ First **SALIVA (1)** sample (2 minutes under the tongue, chew gently) STOP WATCH 2 MINUTES

#### PHYSICAL MEASURES

- ❖ Record height, weight, hip and waist circumference

#### Stress Lab

(check room temperature is 22C)

- ❖ Initialise Finometer and Actiheart : (enter physical data)
- ❖ Attach Actiheart and perform signal test
- ❖ Attach finometer cuffs (middle finger, arm) and height line

#### Rest Period

START CLOCK (Time now.....)

- ❖ Give psychosocial questionnaire (POMS, CES-D)

At min 20 Mood ratings, **SALIVA (2)**

- ❖ Manual blood pressure 1. SBP.....DBP.....

**\*sit quietly for 1 minute\***

- ❖ Manual blood pressure 2. SBP.....DBP.....

At min 75

- ❖ Mood ratings, **SALIVA (3)**

At min 80 begin Stress Tasks, randomise order

#### SPEECH

- ❖ Give written instructions and 2 minutes preparation, time for 3 minutes
- ❖ Task Impact questionnaire

#### MIRROR

- ❖ Give written instructions
- ❖ Explain task, allow to practise (within reason)
- ❖ Tell participant to start tracing and set stopwatch for 5 minutes
- ❖ Task impact questionnaire

Number of tracings ..... Number of errors .....

- ❖ **SALIVA (4)** TIME.....

#### RECOVERY PERIOD

RE - START CLOCK (Time now.....)

At min 20 Mood ratings, POMS questionnaire & **SALIVA (5)**

At min 25 FINISH

### 3.ii) Positive emotional style (PES) measure

Participants were asked to complete the following question each evening before they went to sleep using an online questionnaire (or a written diary). Daily positive emotions were calculated as the sum of indicated\* adjectives; positive emotional style (PES) was the mean of daily ratings.<sup>1</sup>

**How accurately does each of the following adjectives describe how you have felt today?**

**0 (not at all)    1        2        3        4 (extremely accurate)**

Tired  
Calm\*  
Sad  
Full of pep\*  
Hostile  
On edge  
Lonely  
Fatigued  
Lively\*  
Angry  
Cheerful\*  
Tense  
At ease\*  
Unhappy  
Isolated  
Happy\*

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<sup>1</sup> Cohen, S., Doyle, W., Turner, R., Alper, C. & Skoner, D. 2003. Emotional style and susceptibility to the common cold. *Psychosomatic Medicine*, 65, 652-657.



### 3.iii) Mood and task ratings

#### Mood ratings

Please answer the following questions by circling the number that best describes the way you feel.

1. How relaxed do you feel at the moment?

Not at all relaxed      1      2      3      4      5      6      7      Very relaxed

2. How anxious do you feel at the moment?

Not at all anxious      1      2      3      4      5      6      7      Very anxious

3. How stressed do you feel at the moment?

Not at all stressed      1      2      3      4      5      6      7      Very stressed

#### Task impact ratings

Please answer the following questions by circling the number that best describes the way you felt during the task.

1. How difficult did you find the task?

Not at all difficult      1      2      3      4      5      6      7      Very difficult

2. How involved in the task did you feel?

Not at all involved      1      2      3      4      5      6      7      Very involved

3. How well do you think you performed the task?

Not at all well      1      2      3      4      5      6      7      Very well

4. How stressed did you feel during the task?

Not at all stressed      1      2      3      4      5      6      7      Very stressed

5. How much in control of the task did you feel?

Not at all in control      1      2      3      4      5      6      7      Very in control

6. How relaxed did you feel during the task?

Not at all relaxed      1      2      3      4      5      6      7      Very relaxed

### 3.iv) Profile of Mood States, short form

Below is a list of words that describe feelings people have. Please read each one carefully, then choose the response which best describes the extent to which you have had this feeling over the last couple of days.<sup>18</sup>

1=Not at all    2=A little    3=Moderately    4=Quite a bit    5=Extremely

Tense	Muddled
Vigorous*	Lively*
Worthless	Sad
Worn out	On edge
Confused	Cheerful*
Angry	Unworthy
Shaky	Fatigued
Forgetful	Furious
Exhausted	Gloomy
Active*	Sluggish
Unable to concentrate	Bad tempered
Annoyed	Uneasy
Energetic*	Efficient
Hopeless	Resentful
Relaxed*	Listless
Weary	Nervous
Unhappy	Bewildered
Bitter	Alert*

*\*POMS-Vigor Scale*

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<sup>18</sup> Concise version of the Profile of Mood States (McNair, 1971). Previously used by: Steptoe, A., Edwards, S., Moses, J. & Mathews, A. 1989. The effects of exercise training on mood and perceived coping ability in anxious adults from the General population. *Journal of Psychosomatic Research*, 33(5): 537-547.

## Appendix: Chapter 5

### 5.i) BALPA fatigue survey 2010



18 October 2010

### Pilots Survey 2010

#### Introduction

This survey is being conducted by researchers at University College London (UCL). We would like to investigate the characteristics of flight patterns and other work demands which may affect pilot health and well-being.

The survey has been commissioned by BALPA. Participation is voluntary. If you do decide to participate, please return the questionnaire as soon as possible in the attached stamped addressed envelope. **By returning the survey, you are consenting for your responses to be completed in the research.**

#### Are my answers confidential?

The answers to these questions will be kept strictly confidential. Responses will be combined into results about large groups of respondents. It will not be possible to identify any individual responses from reports or publications of the results.

Any personal information that you give for this survey will only be use for the purposes of this survey. Under no circumstances will any information from an individual record be made available to anyone outside the UCL research team.

#### Outline

The survey has 5 sections. It will take approximately 25 minutes to complete. Please answer all questions as honestly and accurately as you can.

To select answer, tick the appropriate box:

Examples:

i) Are you a pilot?	<input checked="" type="checkbox"/>	Yes
(Please tick one)	<input type="checkbox"/>	No

	Strongly agree	Slightly agree	Slightly disagree	Strongly disagree
ii) I enjoy completing surveys	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

If you make a mistake, please cross out the incorrect response, and put a tick the correct box.

## Section 1: Role and recent experiences

The first few questions are about your current role and experience.

1. Where are you based? (Please tick the correct box.)	<input type="checkbox"/>	Belfast
	<input type="checkbox"/>	Bristol
	<input type="checkbox"/>	Edinburgh
	<input type="checkbox"/>	Glasgow
	<input type="checkbox"/>	Gatwick
	<input type="checkbox"/>	Liverpool
	<input type="checkbox"/>	Luton
	<input type="checkbox"/>	Manchester
	<input type="checkbox"/>	Newcastle
	<input type="checkbox"/>	Stansted
	<input type="checkbox"/>	Berlin
<input type="checkbox"/>	Milan	
<input type="checkbox"/>	Rome	
<input type="checkbox"/>	Paris (ORY)	
<input type="checkbox"/>	Paris (CDG)	
<input type="checkbox"/>	Madrid	

2. What is your current rank?	<input type="checkbox"/>	Captain
	<input type="checkbox"/>	First officer

3. How long have you been employed at this level?  
(Please write in the number of years.) \_\_\_\_\_ years (to the nearest whole year)

4. How long have you been flying with your current employer?  
(Please write in.) \_\_\_\_\_ years (to the nearest whole year)

4A. How many years in total have you been working as a pilot?  
(Please write in.) \_\_\_\_\_ years (to the nearest whole year)

We would now like to ask you about your flying experience over the last 6 months.

5. Over the past 6 months, what has been your usual roster pattern? (Please select one option only.)	<input type="checkbox"/>	5-3-5-4
	<input type="checkbox"/>	FRV
	<input type="checkbox"/>	Opt out
	<input type="checkbox"/>	PPY 75
	<input type="checkbox"/>	Part-time 50% split week
	<input type="checkbox"/>	Part-time 50% split month
<input type="checkbox"/>	Part-time 75% split week	
<input type="checkbox"/>	Part-time 75% split month	

6. How many hours have you flown in the last 6 months?	<input type="checkbox"/>	More than 500 hours
	<input type="checkbox"/>	425 - 500 hours
	<input type="checkbox"/>	350 - 424
	<input type="checkbox"/>	Fewer than 350 hours

7. Approximately how often over the last 6 months has discretion been required (whether or not you have exercised it)?	<input type="checkbox"/>	Not at all
	<input type="checkbox"/>	Up to once a month
	<input type="checkbox"/>	2-3 times a month
	<input type="checkbox"/>	Once a week
<input type="checkbox"/>	More than once a week	

8. Have you completed a Fatigue Report Form over the last 6 months?	<input type="checkbox"/>	Yes, I have filed >3 reports
	<input type="checkbox"/>	Yes, I filed 2-3 reports
	<input type="checkbox"/>	Yes, I filed one report
	<input type="checkbox"/>	No, I have not filed one

9. Were there any occasions over the past 6 months when you did not file a fatigue report form, but you think you should have done?	<input type="checkbox"/>	
	<input type="checkbox"/>	Yes
	<input type="checkbox"/>	No (Please skip to Q10 overleaf)

9A. If you answered 'Yes' to Q9 above:  Why didn't you file a Fatigue Report Form? (Please select any reasons that apply.)	<input type="checkbox"/>	
	<input type="checkbox"/>	I could see no benefit in doing so
	<input type="checkbox"/>	I had already filed several reports
	<input type="checkbox"/>	I was too tired
	<input type="checkbox"/>	It was my own fault I was fatigued
	<input type="checkbox"/>	I did not want to make a fuss
	<input type="checkbox"/>	I did not want management to have a less positive perception of me
	<input type="checkbox"/>	None of these

The next few questions are about your work over the last month (28 days).

Over the **last 28 days**,

10. how many <b>duty hours</b> have you completed? (Duty hours refers to both flying time and non-flight duties, including being on standby.)	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>

11. how many <b>hours</b> have you flown?	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>

12. how many <b>sectors</b> have you flown?	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>

13. how many <b>rest days</b> did you have?	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>

14. how many times have you <u>completed</u> 5 consecutive early start duties?	<input type="checkbox"/>	Once
	<input type="checkbox"/>	Twice
	<input type="checkbox"/>	Three times
	<input type="checkbox"/>	Not at all

15. how many times have you <u>completed</u> 5 consecutive evening finish duties?	<input type="checkbox"/>	Once
	<input type="checkbox"/>	Twice
	<input type="checkbox"/>	Three times
	<input type="checkbox"/>	Not at all

15A. how many times have you <u>completed</u> a transition block?	<input type="checkbox"/>	Once
	<input type="checkbox"/>	Twice
	<input type="checkbox"/>	Three times
	<input type="checkbox"/>	Not at all

16. On your <b>most recent</b> flight duty period, did you have to exercise discretion?	<input type="checkbox"/>	Yes
	<input type="checkbox"/>	No

17. On your <b>most recent</b> flight duty period, how many sectors did you complete?	<input type="checkbox"/>	2
	<input type="checkbox"/>	3
	<input type="checkbox"/>	4
	<input type="checkbox"/>	6

18. How long does it usually take you to travel from your home to your base, before starting your duties?	<input type="text"/>	<input type="text"/>
	<input type="text"/>	<input type="text"/>

19. How do you usually travel to and from your base?	<input type="checkbox"/>	I drive myself
	<input type="checkbox"/>	I am driven by someone else
	<input type="checkbox"/>	I take public transport
	<input type="checkbox"/>	I cycle
	<input type="checkbox"/>	I walk

19A. Some pilots may use *fatigue countermeasures* to help them sleep during rest periods or to make them feel more alert during duty hours. For each of the strategies below, please indicate how often – if at all – you use this technique to avoid feeling fatigued at work:  
Please tick one box for each strategy, a) – e)

	Never	Rarely	Some-times	Most FDPs	Every FDP
a) Drinking caffeinated drinks (e.g. coffee, soft drinks)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Taking caffeine supplements (e.g. gum, tablets)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Taking hypnotics to help you sleep (e.g. temazepam, zolpidem, zaleplon or others)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Taking stimulants to help keep you alert (e.g. modafinil, or other legal stimulants)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) Napping in preparation / after a flight	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f) Napping in flight	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## Section 2: Attitudes to work and work life balance

Questions in this section are about what you think and feel about your work.

Some of the questions are similar to each other. Please read each question carefully, and for each question, indicate which option best applies to you. We would like to compare your responses to people working in other professions, so some questions will be more relevant to you than others.

(If you do not have time to complete all the questions now, you can complete the questionnaire over several days.)

*Demand-control* Bosma et al. (1997), Kuper et al. (2003)  
 Demands: items 20a, 20b, 20cr, 22b  
 Control: items 20d-k (r:20g, 20r), 21a-g (r: 21a) (r=reverse coded)

20. Concerning your work:

Please select often or sometimes or rarely or never for each statement.

	Often	Some-times	Rarely	Never, or almost never
a) Do you have to work very fast?				
b) Do you have to work very intensively?				
c) Do you have enough time to do everything?				
d) Do you have the possibility of learning new things through work?				
e) Does your work demand a high degree of skill or expertise?				
f) Does your job require you to take the initiative?				
g) Do you have to do the same thing over and over again?				
h) Do you have a choice in HOW you do your work?				
i) Do you have a choice in deciding WHAT you do at work?				
j) Does your job provide you with a variety of interesting things?				
k) Is your job boring?				

21. About your position at work – how often do the following statements apply to you?

(Please select one answer for every statement.)

	Often	Some-times	Rarely	Never, or almost never
a) Others take decisions concerning my work				
b) I have a good deal of say in decisions about work				
c) I can manage my own pace of working				
d) My working time can be flexible				
e) I can decide when to take a break				
f) I have a say in choosing with whom I work				
g) I have a great deal of say in planning my work environment				

22. About consistency and clarity regarding your job:

(Often / Sometimes / Rarely / Never)

	Often	Some-times	Rarely	Never, or almost never
a) Do you ever get criticized unfairly?				
b) Do different groups at work demand things from you that are hard to combine?				
c) Do you get useful information from your line management?				
d) Do you get consistent information from line management?				
e) Do you ever get praised for your work?				
f) Are you ever treated unfairly at work?				



*Social support*

22c, 22d, 23a, 23b, 23c, 23d

Bosma et al. (1997), Kuper et al. (2003)

23. When you are having difficulties at work:

	Often	Some-times	Rarely	Never, or almost never
a) How often do you get help and support from your colleagues?				
b) How often are colleagues willing to listen to your work related problems?				
c) How often do you get help and support from your immediate superior?				
d) How often is your immediate superior willing to listen to your work related problems?				

24. Do you agree or disagree with each of the following statements?

	Agree	Some-what agree	Some-what disagree	Disagree
a) As soon as I get up the morning, I start thinking about work problems				
b) When I come home, I can easily relax and 'switch off' work				
c) People close to me say I sacrifice myself too much for my job				
d) Work rarely lets me go, it's still on my mind at night				
e) If I postpone something that I was supposed to do today, I will have trouble sleeping at night				

25. To what extent do your job responsibilities interfere with your family life?

Would you say:-

	Not at all	To some extent	A great deal	Does not apply to me
a) Your job reduces the amount of time you can spend with the family				
b) Problems at work make you irritable at home				
c) Your job involves too much travel away from home				
d) Your job takes so much energy you don't feel up to doing things that need attention at home				

26. How satisfied are you with your job as a whole taking everything into consideration?

<input type="checkbox"/>	Very satisfied
<input type="checkbox"/>	Satisfied
<input type="checkbox"/>	Dissatisfied
<input type="checkbox"/>	Very dissatisfied

### Section 3: Health and well-being

In this section we will ask you about your health and well-being. Several questions mention 'fatigue'. Fatigue refers to *extreme tiredness*, which can be caused by mental or physical exertion or illness.

27. Looking back over the last <b>six months</b> at work, how often did you feel you experienced significant fatigue from your job?	<input type="checkbox"/>	3+ times a week
	<input type="checkbox"/>	Two times a week
	<input type="checkbox"/>	Once a week
	<input type="checkbox"/>	Once a fortnight
	<input type="checkbox"/>	Once a month
	<input type="checkbox"/>	Less than once a month
28. During the past <b>six months</b> , to what extent has fatigue interfered with your normal social activities with family, friends, neighbours or groups?	<input type="checkbox"/>	Extremely
	<input type="checkbox"/>	Quite a bit
	<input type="checkbox"/>	Moderately
	<input type="checkbox"/>	Slightly
28A. Also during the past <b>six months</b> , how often have you felt that your abilities were compromised by fatigue whilst in flight?	<input type="checkbox"/>	Not at all
	<input type="checkbox"/>	Once a week or more
	<input type="checkbox"/>	More than once a month
	<input type="checkbox"/>	Several times
29. In the last 6 months, how many days were you unable to fly because of health reasons?	<input type="checkbox"/>	Only once
	<input type="checkbox"/>	Never
	<input type="checkbox"/>	
	<input type="checkbox"/>	_____ days
30. After completing 5 consecutive early start duties, how long does it usually take you to recover from feelings of fatigue?	<input type="checkbox"/>	I would not feel fatigued
	<input type="checkbox"/>	I recover after 1 rest day
	<input type="checkbox"/>	I recover after 2 rest days
	<input type="checkbox"/>	I recover after 3 rest days
31. After completing 5 consecutive evening finish duties, how long does it usually take you to recover from feelings of fatigue?	<input type="checkbox"/>	I return to work still fatigued
	<input type="checkbox"/>	I would not feel fatigued
	<input type="checkbox"/>	I recover after 1 rest day
	<input type="checkbox"/>	I recover after 2 rest days
	<input type="checkbox"/>	I recover after 3 rest days
	<input type="checkbox"/>	I recover after 4 rest days
	<input type="checkbox"/>	I return to work still fatigued

Jenkins Sleep Problems: items 32a-e

Jenkins (1988)

32. How often in the **past four weeks** did you:

	not at all	1-3 days	4-7 days	8-14 days	15-20 days	22-31 days
a) Have trouble falling asleep?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Wake up several times per night?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Have trouble staying asleep (including waking up far too early)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Wake up after your usual amount sleep feeling tired and worn out?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) Have disturbed or restless sleep?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

33. The questions in this scale also ask about your feelings and thoughts over the **past four weeks**. In each case, indicate *how often* you felt or thought a certain way.

	Never	Almost never	Sometimes	Fairly often	Very often
a) How often have you felt that you were unable to control the important things in your life?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) How often have you felt confident about your ability to handle your personal problems?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) How often have you felt that things were going your way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) How often have you felt difficulties were piling up so high that you could not overcome them?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Fatigue Severity Scale: items 34a-1

Krupp et al. (1989)

34. For each of the following statements, please circle a number from 1 to 7, based on how accurately that statement reflects how you have felt over the **past two weeks** and the extent to which you agree or disagree that the statement applies to you.

1= strong disagreement, 7 = strong agreement.

During the **past two weeks** I have found that,

strongly agree strongly disagree

a) My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
b) Exercise makes me feel fatigued.	1	2	3	4	5	6	7
c) I am easily fatigued.	1	2	3	4	5	6	7
d) Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
e) Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
f) My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
g) Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
h) Fatigue is my major concern.	1	2	3	4	5	6	7
i) Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

Hospital Anxiety and Depression Scale

HADS-PA, Positive affect: 35b, 35d, 35f, 35l

HADS-NA, Negative affect: 35a, 35c, 35e, 35m

Zigmond & Snaith (1983)

35. The next series of questions is also about how you have been feeling **over the last two weeks**. You don't have to think too much to answer, spontaneous answers are most important.

Please select one answer for each question:

a) I feel tense or 'wound up':	<input type="checkbox"/>	Most of the time
	<input type="checkbox"/>	A lot of the time
	<input type="checkbox"/>	From time to time, occasionally
	<input type="checkbox"/>	Not at all
b) I still enjoy the things I used to enjoy:	<input type="checkbox"/>	Definitely as much
	<input type="checkbox"/>	Not quite so much
	<input type="checkbox"/>	Only a little
	<input type="checkbox"/>	Hardly at all
c) I get an apprehensive feeling, as if something awful is about to happen:	<input type="checkbox"/>	Very definitely and quite badly
	<input type="checkbox"/>	Yes, but not too badly
	<input type="checkbox"/>	A little, but it doesn't worry me
	<input type="checkbox"/>	Not at all
d) I can laugh and see the funny side of things:	<input type="checkbox"/>	As much as I always could
	<input type="checkbox"/>	Not quite so much now
	<input type="checkbox"/>	Definitely not so much now
	<input type="checkbox"/>	Not at all
e) Worrying thoughts go through my mind:	<input type="checkbox"/>	A great deal of the time
	<input type="checkbox"/>	A lot of the time
	<input type="checkbox"/>	From time to time, but not too often
	<input type="checkbox"/>	Only occasionally
f) I feel cheerful:	<input type="checkbox"/>	Not at all
	<input type="checkbox"/>	Not often
	<input type="checkbox"/>	Sometimes
	<input type="checkbox"/>	Most of the time
g) I can sit at ease and feel relaxed:	<input type="checkbox"/>	Definitely
	<input type="checkbox"/>	Usually
	<input type="checkbox"/>	Not Often
	<input type="checkbox"/>	Not at all

h) I feel as if I am slowed down:	<input type="checkbox"/>	Nearly all the time
	<input type="checkbox"/>	Very often
	<input type="checkbox"/>	Sometimes
	<input type="checkbox"/>	Not at all

i) I get a sort of frightened feeling like 'butterflies' in the stomach	<input type="checkbox"/>	Not at all
	<input type="checkbox"/>	Occasionally
	<input type="checkbox"/>	Quite Often
	<input type="checkbox"/>	Very Often

j) I have lost interest in my appearance:	<input type="checkbox"/>	Definitely
	<input type="checkbox"/>	I don't take as much care as I should
	<input type="checkbox"/>	I may not take quite as much care
	<input type="checkbox"/>	I take just as much care as ever

k) I feel restless, as if I have to be on the move:	<input type="checkbox"/>	Very much indeed
	<input type="checkbox"/>	Quite a lot
	<input type="checkbox"/>	Not very much
	<input type="checkbox"/>	Not at all

l) I look forward with enjoyment to things:	<input type="checkbox"/>	As much as I ever did
	<input type="checkbox"/>	Rather less than I used to
	<input type="checkbox"/>	Definitely less than I used to
	<input type="checkbox"/>	Hardly at all

m) I get sudden feelings of panic:	<input type="checkbox"/>	Very often indeed
	<input type="checkbox"/>	Quite often
	<input type="checkbox"/>	Not very often
	<input type="checkbox"/>	Not at all

n) I can enjoy a good book or radio or TV program:	<input type="checkbox"/>	Often
	<input type="checkbox"/>	Sometimes
	<input type="checkbox"/>	Not often
	<input type="checkbox"/>	Very seldom

NO QUESTION 36

37. Do you, or have you ever, suffered from any of these health conditions? <i>Please select all that apply.</i>	<input type="checkbox"/>	Diabetes
	<input type="checkbox"/>	Hypertension
	<input type="checkbox"/>	Heart disease
	<input type="checkbox"/>	Depression or anxiety
	<input type="checkbox"/>	Asthma
	<input type="checkbox"/>	None of these

38. In general would you say your health is: <i>(Please tick one)</i>	<input type="checkbox"/>	Excellent
	<input type="checkbox"/>	Very good
	<input type="checkbox"/>	Good
	<input type="checkbox"/>	Fair
	<input type="checkbox"/>	Poor

#### Section 4: Diet and exercise

We would like to ask you a few questions about your diet and other health related habits.

For each question, please select the one answer that best describes you.

39. How many portions of fruit or vegetables do you eat per day? <i>1 portion = 1 medium piece of fruit OR 100ml fruit/veg juice OR 3 tablespoons of vegetables, including salad</i>		
<i>Please select an answer for typical:</i>	<i>a) On working days</i>	<i>b) On rest days:</i>
<i>a) working days</i>	<input type="checkbox"/> 5+ portions per day	<input type="checkbox"/> 5+ portions per day
<i>b) rest days</i>	<input type="checkbox"/> 2-4 portions per day	<input type="checkbox"/> 2-4 portions per day
	<input type="checkbox"/> 1 portion per day	<input type="checkbox"/> 1 portion per day
	<input type="checkbox"/> 1 every few days	<input type="checkbox"/> 1 every few days
	<input type="checkbox"/> Rarely or never	<input type="checkbox"/> Rarely or never

40. We are interested in whether or not you smoke cigarettes. <i>Which one of these best describes you?</i>	<input type="checkbox"/>	I smoke cigarettes every day
	<input type="checkbox"/>	I smoke cigarettes sometimes
	<input type="checkbox"/>	I used to smoke, but I've given up
	<input type="checkbox"/>	I have never smoked

41. Do you drink alcoholic drinks, of any kind? <i>Please select one answer.</i>	<input type="checkbox"/>	Yes, I drink alcohol regularly
	<input type="checkbox"/>	Yes, I drink alcohol occasionally
	<input type="checkbox"/>	I drink very occasionally (special occasions only)
	<input type="checkbox"/>	No, I do not drink alcohol
	<input type="checkbox"/>	

## 42. Thinking about the last 6 months:

	Yes	No
a) Have you had a feeling of guilt or remorse after drinking?		
b) Has a friend or a family member told you about things you said or did while you were drinking that you could not remember?		
c) Have you failed to do what was normally expected of you because of drinking?		
d) Do you sometimes take a drink when you first get up in the morning?		

43. During a typical week, how often do you complete at least 30 minutes of sport or exercise?	<input type="checkbox"/>	5 or more days a week
	<input type="checkbox"/>	2 – 4 days a week
	<input type="checkbox"/>	Once a week
	<input type="checkbox"/>	Once every few weeks
	<input type="checkbox"/>	Less than once a month
	<input type="checkbox"/>	Never
<i>(For example, this could include team sports, cycling, going to the gym, jogging or brisk walking.)</i>		

## Section 5: Personal characteristics

In the final section, we would like to ask a few more questions about you.

46. Are you..	<input type="checkbox"/>	Male
	<input type="checkbox"/>	Female

47. How old are you?	<input type="checkbox"/>	20-29
	<input type="checkbox"/>	30-39
	<input type="checkbox"/>	40-49
	<input type="checkbox"/>	50-59
	<input type="checkbox"/>	60+

48. Whom do you live with?	<input type="checkbox"/>	Live alone
	<input type="checkbox"/>	Live with partner
	<input type="checkbox"/>	Live with child(ren) aged <12 months
	<input type="checkbox"/>	Live with child(ren) aged 1-5
	<input type="checkbox"/>	Live with child(ren) aged 6+
<i>Please select all that apply.</i>		

## 50. Time and date of survey completion:

Time: \_\_\_\_\_

Date: \_\_\_\_\_

## 51. Finally, we would like to ask your staff number.

This is so that if your answers indicate that you may benefit from medical advice, we can recommend (confidentially) to you to contact a doctor.

Staff number:

*If you would prefer not to include your staff number, please leave this question blank.*

THANK YOU FOR COMPLETING THIS SURVEY.

PLEASE RETURN THE COMPLETED FORM TO:

BALPA Project  
Psychobiology Group  
Department of Epidemiology & Public Health  
UCL Gower Street Campus  
1 - 19 Torrington Place  
London WC1E 6BT

This project is covered by the UCL Data Protection Registration, reference No. Z6364106/2010/10/13, section 19, research: Health Research.

## Appendix: Chapter 6

### Cortisol monitoring study materials

- 6.i) Newsletter item about the study
- 6.ii) Consent form
- 6.iii) Participant information sheet
- 6.iv) Questionnaire
- 6.v) Cortisol and affect logbook

6.i) Newsletter invitation to participate

### Approach to BALPA members within routine newsletter:

*(BALPA is the British Association of Airline Pilots)*

#### Follow-up to fatigue and well-being survey - Volunteers needed

Results of the recent survey identified concerns about fatigue for some members. To further investigate the drivers of fatigue and the impacts on health, the research team from UCL are now recruiting volunteers for a new study. The study will involve collecting saliva samples and completing a daily diary over several days. Saliva will be analysed to assess levels of the stress hormone, cortisol. The study is open to male pilots working the standard 5-4-5-3 shift pattern, whether or not they are experiencing fatigue.

If you are interested in being involved in the study, or for more information, please email Sophie Bostock, a researcher at UCL: [sophie.bostock.09@ucl.ac.uk](mailto:sophie.bostock.09@ucl.ac.uk).

(Please note that personal data will only be used and stored in accordance with the UK Data Protection Act, 1998.)

UCL DEPARTMENT OF EPIDEMIOLOGY  
AND PUBLIC HEALTH  
PSYCHOBIOLOGY GROUP



VERSION 1, 24 FEBRUARY 2011

UCL Project ID number: 3035/001

Participant ID number:

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Title of study: **Fatigue and well-being in airline pilots**

Chief investigator: **Professor Andrew Steptoe**

Researcher: **Sophie Bostock**

### INFORMED CONSENT FORM

**Please initial box:**

1.	I confirm that I have read and understand the participant information sheet dated 24/2/11 (version 1) for the above study. I have had the opportunity to consider the information and to ask questions via phone or email. Any questions I had were answered satisfactorily.	<input type="checkbox"/>
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my legal rights being affected.	<input type="checkbox"/>
3.	I understand that all the information I provide for the purposes of this study will be kept strictly confidential.	<input type="checkbox"/>
4.	I understand that the researchers will need to know my name, address and contact details. These will be used only to contact me about the study. I give permission for the researchers to have this information.	<input type="checkbox"/>
5.	I understand that the researchers need to link my details to my responses to the BALPA survey of fatigue and well-being, dated October 2010. I give permission for researchers to link these data.	<input type="checkbox"/>
6.	I agree to take part in this study.	<input type="checkbox"/>

Signature of participant  
(Electronic signature or full typed name)

Date



VERSION 1, 24 FEBRUARY 2011

## **PARTICIPANT INFORMATION LEAFLET**

### **Fatigue and well-being in airline pilots**

We would like to invite you to take part in a research study. Please read this leaflet which tells you about the study and what it involves. Please contact us if there is anything that is not clear. Take time to decide whether or not you wish to take part.

#### **What is the purpose of the study?**

This study aims to explore the links between work stress, fatigue and health. Cortisol is a hormone that is released throughout the day but particularly when we are under stress. It can be measured simply by taking saliva samples. We are interested in the possible links between fatigue, work (flight) demands and cortisol levels over the day. It is an important area of research, looking into ways in which stress might affect biological responses related to health.

|

#### **Why have I been chosen?**

In order to standardise the effect of work patterns, we would like to recruit pilots working on the 5-3-5-4 roster (the most common roster pattern). Gender and smoking affect cortisol patterns so to reduce natural variation in the sample we are recruiting male non-smoking pilots. The study is open to UK **BALPA members who completed the UCL survey of fatigue and well-being**, dated October 2010. Although the 2010 fatigue survey was completed anonymously, we would like to use your details to link cortisol information to your earlier survey responses. An additional restriction is that we cannot include people taking any medicines that affect the levels of cortisol (e.g. some anti-inflammatory medicines for asthma and arthritis - if you are unsure



some anti-inflammatory medicines for asthma and arthritis - if you are unsure about whether this includes you, please contact us).

**What does the study involve?**

If you agree to be involved, you will be sent a pack by post containing the study materials: a diary to complete on monitoring days, tubes containing cotton wool (which you will use to collect saliva samples), another short questionnaire and a postage paid envelope to return these items to us.

We would like you to take a series of saliva samples at timed intervals on 2 early shift days, 2 late shift days and 2 rest days. We would prefer the samples to be taken in 2 day 'blocks' (i.e. over 2 consecutive days), but you can leave a break between the blocks to fit your schedule. We will ask you to try and complete all 6 sampling days within a total of two weeks.

- Taking the saliva samples simply involves rolling a special piece of cotton wool in your mouth for one minute and then putting it back in its tube. Each time you take a sample, we will ask you to write down the time and how you were feeling.
- On each sampling day, you will take a sample as soon as you wake up, then (from waking): 30 minutes later, 2.5hrs later, 8hrs later, 12hrs later and bedtime. We will provide you with an instruction booklet to help remind you when to take the samples. If you cannot take a sample at the allotted time, we would like you to try and take it within 30 minutes. If you miss a sample by more than 30 minutes, simply take the next sample at the allocated time.
- The other thing we ask is that you do not drink caffeine (tea, coffee or coke), eat or brush your teeth during the 15 minutes before each sample. Otherwise, we want you to go about your normal day.
- The samples should be stored in a refrigerator until you have completed all 6 days of sampling and then returned to us in the postage paid envelope.

**Do I have to take part?**

It will be entirely up to you to decide whether to take part and you are allowed to pull out of the study at any point. There will be no consequences of withdrawal from the study.

**What happens to the information?**

All the information we get from you, including your name, is completely confidential and will only be used for research purposes. The information from all the volunteers will be combined and no individual information will be able to be identified.

**What are the possible disadvantages of taking part?**

We do not anticipate any disadvantages in participating in this study, except taking up your time to take samples and record the details in the diary.

**What are the possible benefits of taking part?**

Although there may be no direct benefits to you personally, we hope that you find the research an interesting experience. The information we get from this study may also help us to understand the effects of different flight schedules and work stress on fatigue and long-term health. The findings of the study will be shared with BALPA. Your participation to help further this research would be appreciated.

**Will my taking part in this study be kept confidential?**

All the information we get from you, including your name, is completely confidential and will only be used for research purposes. The information from all the volunteers will be combined and no individual's information will be identifiable.

**What will happen to the results of the study?**

Once the study has finished the results will be analysed and we will send you, and BALPA, a summary of the results. Findings may be published in a scientific journal, but the neither the airline nor any individual will be identifiable in academic papers.



**Who is organising and funding the research**

The study has been commissioned by BALPA, the British Association of Airline Pilots. The study is being led by Professor Andrew Steptoe, British Heart Foundation Professor of Psychology and Head of the Psychobiology Group, University College London. The Group's work is also funded by the British Heart Foundation.

**Who has reviewed this study?**

This study has been approved by UCL Research Ethics Committee.

**Contact details**

Please contact Sophie Bostock if you are interested in participating, if you would like to ask questions about the study.

By email: [sophie.bostock.09@ucl.ac.uk](mailto:sophie.bostock.09@ucl.ac.uk)

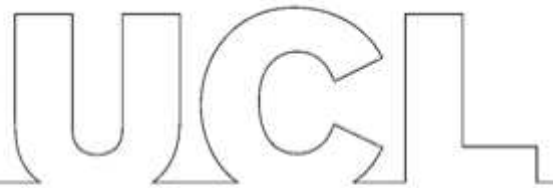
By telephone: 020 7679 8393

By post: 1-19 Torrington Place  
Department of Epidemiology and Public Health,  
University College London  
1-19 Torrington Place,  
London WC1E 6BT

Web-site: [www.ucl.ac.uk/psychobiology](http://www.ucl.ac.uk/psychobiology) .

You can also contact Professor Steptoe on 0207 679 1804 or by email ([a.step toe@ucl.ac.uk](mailto:a.step toe@ucl.ac.uk)).

Thank you very much for taking the time to read this information about the study.



May 2011

### Pilot Fatigue and Well-Being Study 2011

We would like to link your cortisol results to the answers to the questionnaire you completed last autumn. We are also interested in whether your responses to several questions have changed over the last 6 months. Please complete this short questionnaire and return it in the envelope with your cortisol samples and daily diary.

#### Section 1:

**PLEASE COMPLETE THIS SECTION AS YOU WOULD HAVE RESPONDED LAST OCTOBER SO THAT WE CAN MATCH YOU TO YOUR PREVIOUS ANSWERS**

1. How old are you?

<input type="checkbox"/>	20-29
<input type="checkbox"/>	30-39
<input type="checkbox"/>	40-49
<input type="checkbox"/>	50-59
<input type="checkbox"/>	60+

2. Where are you based?  
(Please tick the correct box.)

<input type="checkbox"/>	Belfast	<input type="checkbox"/>	Liverpool
<input type="checkbox"/>	Bristol	<input type="checkbox"/>	Luton
<input type="checkbox"/>	Edinburgh	<input type="checkbox"/>	Manchester
<input type="checkbox"/>	Glasgow	<input type="checkbox"/>	Newcastle
<input type="checkbox"/>	Gatwick	<input type="checkbox"/>	Stansted

3. How long does it take you to travel to work?

<input type="text"/>	min
----------------------	-----

4. What is your current rank?

<input type="checkbox"/>	Captain
<input type="checkbox"/>	First officer

5. How long have you been employed at this level?

(Please write in.)

<input type="text"/>	years (to the nearest whole year)
----------------------	-----------------------------------

6. How long have you been flying with your current employer?

<input type="text"/>	years (to the nearest whole year)
----------------------	-----------------------------------

7. How many years in total have you been working as a pilot?

<input type="text"/>	years (to the nearest whole year)
----------------------	-----------------------------------

\*If you have changed your details since you completed the last questionnaire, please list the changes below:

<input type="text"/>
----------------------

## Section 2: Physical characteristics

Levels of the stress hormone, cortisol, may be related to your BMI (body mass index) or blood pressure. BMI is calculated from your height and weight. If you know your height, weight and/or blood pressure, please enter this information below.

- a) Height  metres OR  feet/inches
- b) Weight  kg OR  stone/lbs
- c) Blood pressure (e.g. 120/80mmHg)  /  last measured  /  (month/year)

If you do not know these details, please leave blank and continue to Section 3.

## Section 3: Attitudes to work and work life balance

Questions in this section are about what you think and feel about your work **now**. Some of the questions are similar to each other. Please read each question carefully, and for each question, indicate which option best applies to you.

### 1. Concerning your work:

*Please select often or sometimes or rarely or never for each statement.*

	Often	Some-times	Rarely	Never, or almost never
a) Do you have to work very fast?				
b) Do you have to work very intensively?				
c) Do you have enough time to do everything?				
d) Do you have the possibility of learning new things through work?				
e) Does your work demand a high degree of skill or expertise?				
f) Does your job require you to take the initiative?				
g) Do you have to do the same thing over and over again?				
h) Do you have a choice in HOW you do your work?				
i) Do you have a choice in deciding WHAT you do at work?				
j) Does your job provide you with a variety of interesting things?				
k) Is your job boring?				

2. About your position at work – how often do the following statements apply?  
(Please mark either *Often* / *Sometimes* / *Rarely* / *Never* for every statement.)

	Often	Some- times	Rarely	Never, or almost never
a) Others take decisions concerning my work				
b) I have a good deal of say in decisions about work				
c) I can manage my own pace of working				
d) My working time can be flexible				
e) I can decide when to take a break				
f) I have a say in choosing with whom I work				
g) I have a great deal of say in planning my work environment				

3. About consistency and clarity regarding your job:

	Often	Some- times	Rarely	Never, or almost never
a) Do you ever get criticized unfairly?				
b) Do different groups at work demand things from you that are hard to combine?				
c) Do you get useful information from your line management?				
d) Do you get consistent information from line management?				
e) Do you ever get praised for your work?				
f) Are you ever treated unfairly at work?				

4. When you are having difficulties at work:

	Often	Some- times	Rarely	Never, or almost never
a) How often do you get help and support from your colleagues?				
b) How often are colleagues willing to listen to your work related problems?				
c) How often do you get help and support from your superior?				
d) How often is your immediate superior willing to listen to work related problems?				

#### Section 4: Sleep and fatigue

Fatigue refers to extreme tiredness, which can be caused by mental or physical exertion or illness.

1. Looking back over the last <b>six months</b> at work, how often did you feel you experienced significant fatigue from your job?	<input type="checkbox"/>	3+ times a week
	<input type="checkbox"/>	Two times a week
	<input type="checkbox"/>	Once a week
	<input type="checkbox"/>	Once a fortnight
	<input type="checkbox"/>	Once a month
	<input type="checkbox"/>	Less than once a month
	<input type="checkbox"/>	Never

2. Also during the past <b>six months</b> , how often have you felt that your abilities were compromised by fatigue whilst in flight?	<input type="checkbox"/>	Once a week or more
	<input type="checkbox"/>	More than once a month
	<input type="checkbox"/>	Several times
	<input type="checkbox"/>	Only once
	<input type="checkbox"/>	Never

3. How often in the **past four weeks** did you:

	not at all	1-3 days	4-7 days	8-14 days	15- 20 days	22- 31 days
a) Have trouble falling asleep?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Wake up several times per night?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Have trouble staying asleep (including waking up far too early)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Wake up after your usual amount sleep feeling tired and worn out?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) Have disturbed or restless sleep?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. For each of the following statements, please *circle a number from 1 to 7*, based on how accurately that statement reflects how you have felt over the **past two weeks** and the extent to which you agree or disagree that the statement applies to you. During the **past two weeks** I have found that.

	strongly disagree-----					strongly agree	
a) My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
b) Exercise makes me feel fatigued.	1	2	3	4	5	6	7
c) I am easily fatigued.	1	2	3	4	5	6	7
d) Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7



e) Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
f) My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
g) Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
h) Fatigue is my major concern.	1	2	3	4	5	6	7
i) Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

### Section 5: Work history – Flight Schedule

Finally, we would like to know about your recent flight history.

The easiest and most reliable way to collect this information is for you to PRINT and ATTACH a copy of an up-to-date log showing your recent Flight/Duty Time totals over the past 12 months (including columns for block hours, duty hours and sectors).

1. How many **duty hours** have you completed **over the last 14 days**?

duty hours

2. How many **flying hours** have you completed **over the last 14 days**?

flight hours

3. How many **sectors** have you flown **over the last 14 days**?

sectors

4. On how many days have you flown into discretionary hours **over the last 14 days**?

days

5. How many **duty hours** have you completed **over the last 6 months**?

duty hours

6. How many **flying hours** have you completed **over the last 6 months**?

flight hours

7. How many **sectors** have you flown **over the last 6 months**?

sectors

8. On how many days have you flown into discretionary hours **over the last 6 months**?

days



**Pilot Fatigue and  
Well-Being Study  
Cortisol Diary**

**CONFIDENTIAL**

Participant study code: \_\_\_\_\_

This diary is to help you to collect saliva samples at timed intervals. It will also provide us with important information that will help us analyse the results.

**Any questions?**

Please email [sophie.bostock.09@ucl.ac.uk](mailto:sophie.bostock.09@ucl.ac.uk) or call on 0207 679 8393.  
(If no reply, please leave a message and we will get back to you.)

**6.v) Cortisol and affect logbook (1 day only included)**

**Instructions for taking saliva samples**

**The night before each collection day, please put the first tube, pen and this logbook close to your bed.**

1. Before each saliva sample, have a 'clean' mouth for at least 15 minutes before you take the sample (no eating, brushing teeth, or drinks, including water).
2. Take the lid off the tube – try not to handle the cotton swab with your hands.
3. Tip the swab into your mouth and chew gently until the cotton is soaked. This usually takes about 1 minute.
4. While you are letting it soak in your mouth, write the DATE and TIME OF SAMPLE on the tube label. Then fill in the relevant section in this diary.
5. Place the cotton back into the tube and put the lid back on securely. Store in a cold place/fridge as soon as possible. (Cortisol is stable at room temperature, but is best stored at a lower temperature.)

***It may be helpful to set an alarm on your watch or mobile to remember the sampling times.***

**If you miss any samples by more than 30 minutes, please write this on the schedule and take the next one as planned.**

## Planning your Sampling Days

We would like you to take samples in **3 sampling blocks**:

- Early starts (2 days) ● Late starts (2 days) ● Rest days (2 days)

For each block, please take samples over *two consecutive* days.  
You may leave a gap of up to a week between the two-day blocks.

In total, this means you will collect samples for 6 days, which may be spread over up to 20 days.

It does not matter in which order you complete the blocks, i.e. you can choose a two-day block of rest days, followed by a two-day block of early starts, followed by a two-day block of late starts.

On each sampling day, we would like you to take a sample as soon as you **wake up**, then again at the following intervals after waking: **30min**, **2.5hrs**, **8hrs**, **12hrs** and **bedtime**.

For example:

	Wake-up	+30min	+2.5hr	+8hr	+12hr	Bedtime
Tube Number*	1	2	3	4	5	6
Time of Sample	06:00	06:30	08:30	16:30	18:00	23:00

The table overleaf may help you to plan your daily sampling schedule.

*\*Please note: all tubes have the same contents. They have been labelled to help you keep track of your schedule. If you use the wrong tube by mistake, clearly re-label the tube with the correct sample number, time and date.*

Sample Timing Schedule

Wake-up	+30 min	+2.5hr	+8 hr	+12hr	Bedtime
1	2	3	4	5	6
04:30	05:00	07:00	12:30	16:30	
04:45	05:15	07:15	12:45	16:45	
05:00	05:30	07:30	13:00	17:00	
05:15	05:45	07:45	13:15	17:15	
05:30	06:00	08:00	13:30	17:30	
05:45	06:15	08:15	13:45	17:45	
06:00	06:30	08:30	14:00	18:00	
06:15	06:45	08:45	14:15	18:15	
06:30	07:00	09:00	14:30	18:30	
06:45	07:15	09:15	14:45	18:45	
07:00	07:30	09:30	15:00	19:00	
07:15	07:45	09:45	15:15	19:15	
07:30	08:00	10:00	15:30	19:30	
07:45	08:15	10:15	15:45	19:45	
08:00	08:30	10:30	16:00	20:00	
08:15	08:45	10:45	16:15	20:15	
08:30	09:00	11:00	16:30	20:30	
08:45	09:15	11:15	16:45	20:45	
09:00	09:30	11:30	17:00	21:00	

(The time at which you try to go to sleep.)



## 1 EARLY: DAY ONE, Wake-up Please take this sample while still in bed

1. Date today:  /  / 2011  
(Date / Month)

2. Time of sample: Hours :  :   
(24hr clock) Please also write on the tube label.

3. What time did you wake up?  
(24hr clock)  :


4. Did you sleep well last night?  
(Tick one response.)  
☐ Yes, I slept well  
☐ Quite well  
☐ No, I didn't sleep well

*Please avoid having caffeinated drinks until after sample #2 (in 30 minutes).  
You may eat breakfast or brush your teeth now, but please avoid doing this for 15 min before sample #2.*

## 2 EARLY: DAY ONE Waking +30min

1. Time of sample: Hours :  :   
(24hr clock) Please also write on the tube label.

2. In the last 30 minutes, have you felt:

Not at all  Extremely

i. Happy ☐ ☐ ☐ ☐ ☐

ii. Stressed ☐ ☐ ☐ ☐ ☐

iii. Tired ☐ ☐ ☐ ☐ ☐

3. How noisy is it at the moment?

 Silent ☐ ☐ ☐ ☐ ☐ Extremely noisy

4. In the last 15 minutes have you had anything to eat or drink?


☐ Yes ☐ No

☐  
Thank you. Your next sample is due in 2 hours.

## 3 EARLY: DAY ONE Waking +2.5hrs

1. Time of sample:  :   
Please also write on the tube label.

2. In the last 30 minutes, have you felt:


Not at all  Extremely

Happy ☐ ☐ ☐ ☐ ☐

Stressed ☐ ☐ ☐ ☐ ☐

Tired ☐ ☐ ☐ ☐ ☐

3. How noisy is it?


 Silent ☐ ☐ ☐ ☐ ☐ Extremely noisy

Your next sample is in 5.5hr.

## 4 EARLY: DAY ONE Waking +8hrs

1. Time of sample:  :   
Please also write on the tube label.

2. In the last 30 minutes, have you felt:


Not at all  Extremely

Happy ☐ ☐ ☐ ☐ ☐

Stressed ☐ ☐ ☐ ☐ ☐

Tired ☐ ☐ ☐ ☐ ☐

3. How noisy is it?


 Silent ☐ ☐ ☐ ☐ ☐ Extremely noisy

Your next sample is in 4hr.

## 5 EARLY: DAY ONE Waking +12hrs

1. Time of sample:  :   
Please also write on the tube label.

2. In the last 30 minutes, have you felt:


Not at all  Extremely

Happy ☐ ☐ ☐ ☐ ☐

Stressed ☐ ☐ ☐ ☐ ☐

Tired ☐ ☐ ☐ ☐ ☐

3. How noisy is it?

 Silent ☐ ☐ ☐ ☐ ☐ Extremely noisy

*Please take your final sample today before bed.*

# 6

## EARLY: DAY ONE Bedtime (final) sample Please take this sample before brushing your teeth

1. Time of sample:  
(24hr clock)

 : 

Please also  
write on the  
tube label.

2. In the last 30 minutes, have you felt:

	Not at all				Extremely
i. Happy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ii. Stressed	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
iii. Tired	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

3. How noisy is it at the moment?

	Silent			Extremely noisy
	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

4. In the last 15 minutes have you had anything to  
eat or drink?

☐ Yes ☐ No

5. Did you drink any alcoholic drinks today?

☐ Yes ☐ No

6. Did you do more than 10 min vigorous  
exercise today? (Exercise that made you sweat  
and/or raised your heart rate.)

☐ Yes ☐ No

Finally today, we would like to know about your  
work patterns.

7. How duty hours did you work?  hrs

8. How many hours did you fly?  hrs

9. How many sectors?  sectors

10. Did you exercise discretion?

☐ Yes ☐ No

*Thank you. Please leave this booklet, a tube  
and a pen by your bed for tomorrow.*

## **Appendix: Chapter 8**

### **Pilot study materials**

- 8.i) Pilot study participant information sheet
- 8.ii) Pilot study consent form
- 8.iii) Pilot study questionnaire

### **RCT materials**

- 8.iv) Trial recruitment poster
- 8.v) Trial screening questionnaire
- 8.vi) Trial participant information sheet
- 8.vii) Trial consent form
- 8.viii) Trial questionnaire
- 8.ix) Trial hair questionnaire
- 8.x) Trial blood pressure and mood diary

### **Supplementary RCT results**

- 8.xi) CONSORT flow diagram for each Site
- 8.xii) Effects of allocation to app vs. wait-list group on outcomes within each site
- 8.xiii) Effects of meditation practice time on blood pressure within each site
- 8.xiv) Outcomes at T3 (10 weeks post intervention)
- 8.xv) Qualitative app feedback

9th December 2011

### **Mindfulness and Work Stress Pilot Study Participant Information**

We're looking for volunteers to take part in a pilot study to investigate whether a mindfulness meditation programme, delivered via a smartphone, can reduce perceptions of work-related stress. The pilot study also aims to identify ways to improve the basic app, based on user feedback.

**What is mindfulness?** Mindfulness is a way of paying attention to the present moment by using meditation and breathing techniques. It involves consciously bringing awareness to your thoughts and feelings, without making judgements about them. Mindfulness is a quality or skill which we all possess to some extent, but that can be developed through practice.

#### **Who can take part?**

Adults who use an iPhone and have recently felt stressed about their work can take part. *Since the study focuses on work-related stress, if you are planning more than 3 days holiday from 9<sup>th</sup>-23<sup>rd</sup> January, we would prefer that you did not take part.*

#### **What happens if I decide to take part?**

##### **1. Complete a well-being questionnaire by 16<sup>th</sup> December**

When you email the research team, you will be sent a hyperlink to an online questionnaire. You will be asked to provide your consent to take part. The questionnaire takes 10-15 minutes to complete. Then you can forget about the study until after Christmas..

##### **2. 'Take 10': meditate for 10 minutes a day, for 10 days in January**

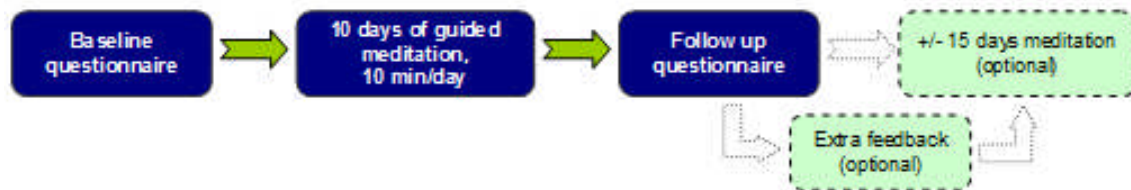
You'll receive an email with instructions to download the app in the first week of January. We'd like you to listen to a 10 minute guided meditation (podcast) every day for 10 days. You can choose when and where to do this. You just need a quiet space where you can sit for 10 minutes without being disturbed.

##### **3. Complete a follow-up questionnaire**

After you've completed the 10 day programme, we'll ask you to complete a follow-up questionnaire online. We might invite you to give additional feedback via a phone interview or focus group, but this is optional. You'll also be offered the chance to continue with a further 15-day meditation programme, if you'd like to.



#### Study sequence



#### What are the potential benefits? Will it work?

NICE (the National Institute for Clinical Excellence), recommends mindfulness-based therapies for patients with recurrent depression. Several research studies have also found benefits in stress reduction for healthy working populations, including reduced burnout and improved relationships with colleagues. Research has found that mindfulness is associated with emotional intelligence, concentration, productivity and leadership ability. However, most of the existing evidence for mindfulness-based therapy is based on intensive group-based programmes. We want to find out whether you can get similar benefits from an internet-based programme, based on short daily practices.

#### Are there any disadvantages to taking part?

There is no evidence that mindfulness-based therapies are harmful. The main disadvantage is the time needed to set aside for completing the daily meditations and questionnaires. If you are too busy you can return to the programme the following day. You have the right to withdraw from the study at any time.

#### What happens to the data?

All the information we get from you, including your name, is completely confidential. We will use the results to improve the app. If the findings are published in a scientific journal or thesis, no individual will be identifiable. All data will be collected and stored in accordance with the Data Protection Act 1998.

#### Who is organising the research?

The app has been created by Headspace, a company specialising in mindfulness meditation. You can find out more about Headspace online at [www.getsomeheadspace.com](http://www.getsomeheadspace.com) – but please don't start meditating just yet! The pilot study is being conducted by researchers from the Psychobiology Group at UCL.

**To take part, please email [mindfulapp@gmail.com](mailto:mindfulapp@gmail.com)  
with 'TAKE PART' in the subject line**

#### Contact details

Please contact the research team if you would like to ask questions about the study.

By email: [mindfulapp@gmail.com](mailto:mindfulapp@gmail.com)

By telephone : Sophie Bostock 07779 578733

Thank you very much for taking the time to read this information about the study.

UCL DEPARTMENT OF EPIDEMIOLOGY  
AND PUBLIC HEALTH  
PSYCHOBIOLOGY GROUP



**Title of study: Mindfulness and Work Stress Pilot Study**

### INFORMED CONSENT

1.	I confirm that I have read and understand the participant information sheet dated 09/12/11. I have had the opportunity to consider the information and to ask questions.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.	
3.	I understand that all the information I provide for the purposes of this study will be kept strictly confidential.	
4.	I understand that the researchers need to know my name and contact details. These will be used only to contact me about the study.	
6.	By completing this online survey, I am consenting to participate in the research.	

Participant's full name

Contact email address





Social support: items 27-31 (30r)

Unden et al. (1991)

The next few questions are about your relationships with work colleagues.

**Response: Strongly disagree (1) — — — — (4) Strongly agree**

- 27. I have a good relationship with my line manager(s).
- 28. I get on well with my co-workers.
- 29. There is a pleasant atmosphere at my workplace.
- 30. There are often conflicts and arguments at work.
- 31. There is good group cohesion at my workplace.

We'd now like to know about how you've been feeling more generally, outside of work.  
This section is about your health and wellbeing.

CES-D: items 32-39

Radloff (1977)

The questions in this scale ask you about your thoughts and feelings over the last two weeks.  
Try to answer each question fairly quickly, selecting whichever answer seems a reasonable estimate.

**Response: None or almost none of the time (1) — — — — (4) All or almost all of the time**

How often in the last two weeks have you...

- 32. ...felt depressed?
- 33. ...felt everything you did was an effort?
- 34. ...felt your sleep was restless?
- 35. ...felt happy?
- 36. ...felt lonely?
- 37. ...felt you enjoyed life?
- 38. ...felt sad?
- 39. ...felt you could not get going?

Great, thank you. Only a couple more questions to go.

Warwick Edinburgh Mental Well-being Scale: items 40-53

Tennant et al. (2007)

Still thinking about how you've been feeling over the last 2 weeks...

**Response: 0=None of the time; 1=Rarely; 2=Some of the time; 3=Often; 4=All of the time**

- 40. I've been feeling optimistic about the future.
- 41. I've been feeling useful.
- 42. I've been feeling relaxed.
- 43. I've been feeling interested in other people.
- 44. I've had energy to spare.
- 45. I've been dealing with problems well.
- 46. I've been thinking clearly.
- 47. I've been feeling good about myself.
- 48. I've been feeling close to other people.
- 49. I've been feeling confident.
- 50. I've been able to make up my own mind about things.
- 51. I've been feeling loved.
- 52. I've been interested in new things.
- 53. I've been feeling cheerful.

54. The mindfulness practice we'd like you to try out can be completed in addition to other meditation or relaxation techniques.

Do you regularly practise any other forms of meditation or physical relaxation techniques?  
**Yes - I regularly practice meditation, yoga, tai chi or something similar**  
**I have done in the past, but not at the moment**  
**No, I've never attempted anything like this before**

55. How confident are you that you will be able to set aside 10 minutes to meditate every day?  
**Not at all confident (1) — — — — (5) Very confident**

56. How confident are you that listening to the mindfulness meditation programme will change the way you feel about work?  
**Not at all confident (1) — — — — (5) Very confident**

OK, this is the final set of questions.

The purpose is to capture your current experiences of mindfulness. Thinking about the last two weeks, pick an answer for each statement as best you can.

Freiburg Mindfulness Inventory: items 57-63

Walach et al. (2006)

There are no 'right' or 'wrong' answers, or 'good' or 'bad' responses. What is important to us is your own personal experience.



**Response: Rarely=1; Occasionally=2; Fairly often=3; Almost always=4**

- 57. I am open to the experience of the present moment.
- 58. I pay attention to what's behind my actions.
- 59. I see my mistakes and difficulties without judging them.
- 60. I am friendly to myself when things go wrong.
- 61. In difficult situations, I can pause without immediately reacting.
- 62. I experience moments of inner peace and ease, even when things get hectic and stressful.
- 63. I watch my feelings, without getting lost in them.

\*\*\*\*\*

Follow-up only:

64. How frequently have you used the app over the last two weeks?
- I didn't download the app (owing to technical or other reasons)**  
**I listened to a few days, but stopped after that**  
**I meditated regularly at the beginning, but tailed off or had long gaps in my practice**  
**I meditated quite regularly, between 2 and 4 days a week (on average)**  
**I meditated routinely, 5 or more days per week (on average)**

65. How much time (in minutes) have you spent meditating over the past two weeks?

\_\_\_\_\_ min

66a. You mentioned that you had no downloaded the app or stopped after a few days.  
Please explain why. (Open question.)

66b. Do you think the time you have spent using the Headspace app over the last 8 weeks has made any difference to the way you think or feel now?  
Please type in a few words or sentences about any changes you've noticed, positive or negative (Open question.)

66c. Finally, we'd like to improve the experience for Headspace users.  
We'd be really grateful for your suggestions. For example, these might be to do with the download or login process, audio or video content, reminders, design, the website - anything which occurs to you.  
(Open question.)



# WE WANT YOU

8.iv) Trial  
recruitment  
poster (Site A)

**Would you like to find out if a mobile app can help  
reduce your stress and enhance your well-being?**

We are looking for 100 people based at Hexagon Place to take part in an innovative study created in collaboration with Roche.

**What will I be doing?**

You will be learning a technique known as mindfulness, a form of mental training that has been shown to reduce anxiety, improve self-control and enhance concentration.



Over a period of 8 weeks, for around 10 minutes a day, you'll be trained using an android or iphone app which will also collect data and provide you with feedback. We'll meet with you before and after the training period and measure your blood pressure. The data will be completely anonymous.

**Interested?**

Click here: [www.wellbeingapp.info](http://www.wellbeingapp.info) and enter the username and password "roche2012" to complete a 3 minute screening questionnaire

The research team will be onsite on Tuesday 7th March outside the restaurant to answer questions. In the meantime please contact us at [wellbeingapp@gmail.com](mailto:wellbeingapp@gmail.com).

The study has been approved by Roche Governance Committee and UCL Research Ethics Committee.

We hope you'll take part.

Thanks,

Sophie Bostock  
British Heart Foundation PhD Fellow  
UCL Psychobiology Group  
[mindfulapp@gmail.com](mailto:mindfulapp@gmail.com)



### Screening Questionnaire

To try and ensure a broad range of participants and to exclude applicants:

a) treated for mental health issues, b) treated for hypertension, c) without depressive symptoms or overcommitment AND d) already meditating on a routine basis.

1. Welcome to the registration survey. We're delighted that you've come this far.

Please read the statements below.

- I've read the study information on the website or downloaded the information sheet.
- I know that if I complete this survey, it doesn't mean that I have to take part in the trial.
- I understand that all my answers will be kept strictly confidential.

Please type in your name below if you agree with these statements.

First name and surname \_\_\_\_\_

2. Perfect, thanks. We'll start with a few general questions, and then move on to a couple more questions about your work and current stress levels.

Are you,

☐ Male

☐ Female

3. How old are you?

years

4. Are you,

☐ employed full-time

☐ employed part-time

5. How would you describe your level of seniority at work on a scale of 1-10, if 10 represents the most senior managers in the UK and 1 represents the most junior employees?

Most junior (1) \_\_\_\_\_ (10) Most senior

6. Participants will be randomised either to start using the app on September 10th (first group), or to start two months later (second group).

Will you accept whichever group you are allocated to?

☐ Yes, I understand that my group will be decided at random

☐ No, I definitely don't want to wait until November to start the mindfulness programme

7. Baseline appointments will take place at both the X campus and the Y campus from 20<sup>th</sup> August to 6<sup>th</sup> September.

Where would you prefer to have an appointment?

☐ X Campus

☐ Y Campus

8. The first app group will be invited to a special launch event with a mindfulness expert. This will be a one hour session.

A possible slot for this meeting is 10am Monday 10th September.  
If you were invited, do you think you would be able to attend the session?  
(We realise your availability may change closer to the event.)

- ☐ I would prefer NOT to attend a group session
- ☐ I'd like to attend but I'm not available on the 10th September
- ☐ I would prefer to attend an event at X campus
- ☐ I would prefer to attend an event at Y campus

Overcommitment: items 9-14 (11r)

Kuper et al. (2002)

We'd like to get an idea about how work stress is affecting you.  
Don't spend too long over each question, go with your instincts and please answer honestly.  
How much do you agree or disagree with each of the following statements?  
1=strongly disagree, 2=disagree, 3=agree, 4=strongly agree

- 9. I get easily overwhelmed by time pressures at work.
- 10. As soon as I get up in the morning I start thinking about work problems.
- 11. When I get home, I can easily relax and 'switch off' work.
- 12. People close to me say I sacrifice too much for my job.
- 13. Work rarely lets me go, it's still on my mind when I go to bed.
- 14. If I postpone something that I was supposed to do today I'll have trouble sleeping at night.

15. Are you currently receiving medical treatment for any of the following conditions?

- ☐ High blood pressure (hypertension)
- ☐ Depression
- ☐ Anxiety
- ☐ Any condition that requires steroid medication e.g. prednisolone
- ☐ None of these

CES-D: items 16-23

Radloff (1977)

The questions in this scale ask you about your thoughts and feelings over the last week. Try to answer each question fairly quickly, selecting yes or no, whichever answer seems most appropriate to you.

Much of the time during the last week you...

- 16. ☐ felt depressed?
- 17. ☐ felt everything you did was an effort?
- 18. ☐ felt your sleep was restless?
- 19. ☐ felt happy?
- 20. ☐ felt lonely?
- 21. ☐ felt you enjoyed life?
- 22. ☐ felt sad?
- 23. ☐ felt you could not get going?

You're very nearly finished. Only three questions to go.

24. We'd like to investigate changes in the stress hormone, cortisol, by cutting a small sample of hair from the back of your head before and after the trial period. The amount we need is about the same thickness as half the diameter of a pencil. You can still take part in the study if you don't want to give a hair sample.

Please read every statement below and select all the statements that apply to you.

- ☐ I have hair longer than 1cm in length on the back of my head
- ☐ I have very short hair (<1cm), or no hair, on the back of my head
- ☐ I would prefer not to have a hair sample taken

25. The intervention we'd like you to trial can be used in addition to other techniques which are designed to reduce stress.

Do you practise any meditation or physical relaxation techniques, such as yoga, at least once a week?

- ☐ Yes - I regularly practice meditation, yoga, tai chi or something similar
- ☐ I have done in the past, but not at the moment
- ☐ No, I have never attempted anything like that

26. How confident are you that you will be able to listen to a podcast most days for 10-20 minutes during the trial?

Not very confident (1) \_ \_ \_ \_ (5) Very confident

27. We'll let you know via email whether you're invited to participate in the trial.

Please type your email address carefully into the box below.  
(Please use a contact email address which you check regularly.)

Contact email address \_\_\_\_\_

Brilliant! Thank you for completing the screening questionnaire.

We'll be in touch by Friday 7th September to let you know whether you're invited to take part in the trial.





26<sup>th</sup> February 2012

### Well-being at Work: Information for Participants

We're looking for volunteers to take part in a research trial to investigate a mobile app which is designed to reduce stress and promote well-being.

#### Who can take part?

You can take part if you have experienced stress at work recently, are generally in good health and use an Android smartphone or iPhone. We will invite 100 Roche employees based at Hexagon Place to participate.

#### What will I have to do?

1. Fill in a screening questionnaire
2. Meet the researcher onsite for a pre-trial interview for 20-25 min (19<sup>th</sup> March – 4<sup>th</sup> April)
3. Take part in the 8-week trial, starting on 18<sup>th</sup> April
4. Meet the researcher again after the trial

Click here to take part: [www.wellbeingapp.info](http://www.wellbeingapp.info)

Enter the username and password 'roche2012'.

We'll invite you to a 20-25min interview where you will complete a questionnaire about stress, well-being and lifestyle. The researcher will take a small sample of hair from the back of your head which we analyse to measure cortisol, a stress hormone. We will show you how to use a small blood pressure monitor on your wrist and ask you to take 4 more readings over 24 hours.

You will be placed at random into one of 2 groups:

- Group 1 will be able to download the app. It consists of a series of daily podcasts, lasting 10-20min each. The aim is to develop mindfulness. We would like you to listen to a new podcast every day – or as often as you can – at a time of your choice.
- Group 2 will wait for 8 weeks before they download the app.

After 8 weeks, we will invite you to another appointment to repeat the pre-trial measurements. After this appointment, **group 2 will also get access to the app**. There will be more questionnaire measures at 4 and 6 months.

#### What are the benefits? Will it work?

You will be learning a technique known as mindfulness, a form of mental training that may influence anxiety, self-control and attention. You will receive feedback from the app and on your blood pressure and cortisol levels. After the study we will send you a summary of the research findings.

#### Are there any disadvantages to taking part?

The main disadvantage is the time needed to set aside for listening to the daily podcasts (10 – 20 mins) and attending interviews before and after the trial (20 mins each). If you are too busy you can skip a podcast and return to the programme the next day. You can withdraw from the study at any time.

#### What happens to the data?

All the information we get from you is confidential and will not be shared with Roche, or any other organisation. If the findings are published in a scientific journal or thesis, no individual will be identifiable. All data will be collected and stored in accordance with the Data Protection Act 1998.

#### Who is organising the research?

The trial is being organised by researchers from the Psychobiology Group at UCL, in collaboration with the company who developed the app. The research team is part-funded by the British Heart Foundation. Roche Governance Committee has agreed for Roche employees based at Hexagon Place to participate. The study has been approved by UCL Research Ethics Committee.

#### Contact details

Please contact the research team if you have any questions about the study.

By email: [wellbeingapp@gmail.com](mailto:wellbeingapp@gmail.com)

By telephone: Sophie Bostock 07779 578733

In person: Hexagon Place, Wednesday 7<sup>th</sup> March – exhibition space

Thank you very much for taking the time to read this information.

**If you would like to take part, please complete the screening questionnaire at:**

[www.wellbeingapp.info](http://www.wellbeingapp.info)

**Type in the username & password: roche2012**

Registration will close on Wednesday 14<sup>th</sup> March

UCL DEPARTMENT OF EPIDEMIOLOGY  
AND PUBLIC HEALTH  
PSYCHOBIOLOGY GROUP



### CONSENT FORM

**Title of study:** Well-being at work: a randomised controlled trial

**Project ID:** 3035/002

This study has been approved by the UCL Research Ethics Committee.

Please complete this form after you have read the Information Sheet dated 26<sup>th</sup> February and had the opportunity to ask questions.

**Participant's Statement:**

I,

*Please write in full name*

- have read the notes written above and the Information Sheet, and understand what the study involves.
- understand that if I decide at any time that I no longer wish to take part in this project, I can notify the researchers involved and withdraw immediately.
- consent to the processing of my personal information for the purposes of this research study.
- understand that such information will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998.
- agree that the research project named above has been explained to me to my satisfaction and I agree to take part in this study.

Date:

Participant's signature:

Researcher's signature:

Participant ID: W A \_ \_ \_

## RCT Baseline Questionnaire

1. Initials \_ \_
2. Study ID GA \_ \_ \_ \_
3. Height \_ metres
4. Weight \_ kg

\*\*\*\*\*

Welcome to the 'Well-being at Work' baseline questionnaire.  
Thanks again for taking part.

This questionnaire is in three main sections. We start with a section about your general well-being, then move on to questions about work and finally a section about your health.  
Please answer every question honestly. All your answers are confidential.

\*\*\*\*\*

Warwick Edinburgh Mental Well-being Scale: items 5-18

Tennant et al. (2007)

5-18. We kick off with a question about your positive thoughts and feelings over the last two weeks. As with all the questions in the survey, don't spend too long over each answer - go with your instincts.

0=None of the time; 1=Rarely; 2=Some of the time; 3=Often; 4=All of the time

I've been feeling optimistic about the future.  
I've been feeling useful.  
I've been feeling relaxed.  
I've been feeling interested in other people.  
I've had energy to spare.  
I've been dealing with problems well.  
I've been thinking clearly.  
I've been feeling good about myself.

Still thinking about the last few weeks..

I've been feeling close to other people.  
I've been feeling confident.  
I've been able to make up my own mind about things.  
I've been feeling loved.  
I've been interested in new things.  
I've been feeling cheerful.

\*\*\*\*\*

No question 19-23.

Freiburg Mindfulness Inventory: items 23-36

Walach et al. (2006)

23-36. OK, now for something a bit different. The purpose is to capture your current experiences of 'mindfulness'. Thinking about the last two weeks, pick an answer for each statement as best you can. There are no 'right' or 'wrong' answers, or 'good' or 'bad' responses. What is important is your own personal experience.

Rarely=1; Occasionally=2; Fairly often=3; Almost always=4

I am impatient with myself and others.  
I am open to the experience of the present moment.  
I see my mistakes and difficulties without judging them.  
I pay attention to what's behind my actions.  
When I notice an absence of mind, I gently return to the experience of the here and now.  
I am friendly to myself when things go wrong.  
In difficult situations, I can pause without immediately reacting.  
I experience moments of inner peace and ease, even when things get hectic and stressful.  
I watch my feelings, without getting lost in them.  
I accept unpleasant experiences.  
I feel connected to my experience in the here-and-now.  
I am able to smile when I notice how I sometimes make life difficult.  
I am able to appreciate myself.  
I sense my body, whether eating, cooking, cleaning or talking.

Demand-control

Demands: items 37-40 (40r); Control: items 41-52 (43r, 51r, 52r)

Bosma et al. (1997)

(r=reverse coded)

Now for section two, which is about your work.

Read each question carefully - we're not trying to catch you out, but some of the questions are quite similar to each other. When it comes to the answers, don't spend too long over each question, give it your 'best guess'.

Often / Sometimes / Rarely / Never, or almost never

37. Do you have to work very fast?
38. Do you have to work very intensively?
39. Do different groups at work demand things from you which you find hard to combine?
40. Do you have enough time to do everything?
41. Do you have a choice in deciding HOW you do your work?
42. Do you have a choice in deciding WHAT you do at work?
43. Others take decisions concerning my work.
44. I have a say in my own work speed.
45. My working time can be flexible.
46. I have a great deal of say in planning my work environment.
47. I can decide when to take a break.
48. I have a good deal of say in decisions about work.
49. Does your work demand a high level of skill and expertise?
50. Does your job require you to take the initiative?
51. Do you have to do the same thing over and over again?
52. Is your job boring?



Social support: items 53-57 (56r)

Unden et al. (1991)

53-57. The next few questions are about your relationships with work colleagues.

Strongly disagree (1) \_ \_ \_ \_ (4) Strongly agree

I have a good relationship with my line manager(s).

I get on well with my co-workers.

There is a pleasant atmosphere at my workplace.

There are often conflicts and arguments at work.

There is good group cohesion at my workplace.

58. On average over the last month, how many hours would you estimate that you have spent working per week?

\_ more than 55 hours

\_ 46-55 hours

\_ 38-45 hours

\_ 37 or fewer

59. How many days do you think you've been off work because of stress or illness over the last 8 weeks?

If you can't remember, give your best estimate.

\_ \_ days

60. Good news - you've completed the section on work stuff (phew!).

We'd now like to know about how you've been feeling more generally, outside of work.

This section is about your physical and mental health.

Do you smoke?

\_ No, I have never smoked

\_ I used to, but I have given up

\_ I do smoke sometimes

If you smoke, how many cigarettes have you smoked over the last 7 days?

\_ \_ (estimate)

61. Over the last 7 days, on how many days have you completed 30 minutes or more of physical exercise?

For example, this could include team sports, exercising in the gym, jogging, cycling or brisk walking.

\_ None

\_ 1 to 2

\_ 3 to 4

\_ 5 to 6

\_ Every day

Jenkins Sleep Problems: items 62-65

Jenkins (1988)

62-65. How often in the past month did you:

Not at all / 1-3 days / 4-7 days / 8-14 days / 15-21 days / 22-31 days

Have trouble falling asleep?

Wake up several times per night?

Have trouble staying asleep (including waking up far too early)?

Wake up after your usual amount of sleep feeling tired and worn out?

Hospital Anxiety and Depression Scale

HADS-A: items 66, 68, 70, 72, 74, 76, 78

HADS-D: items 67, 69, 71, 73, 75, 77, 79

Zigmond & Snaith (1983)

The next series of questions is also about how you have been feeling over the last two weeks. You don't have to think too much to answer, spontaneous answers are most important.

66. I feel tense or 'wound up'

Most of the time / A lot of the time / From time to time, occasionally / Not at all

67. I still enjoy the things I used to enjoy.

Definitely as much / Not quite as much / Only a little / Hardly at all

68. I get an apprehensive feeling, as if something awful is about to happen.

Very definitely and quite badly / Yes, but not too badly / A little, but it does not worry me / Not at all

69. I can laugh and see the funny side of things.

As much as I always could / Not quite so much now / Definitely not so much now / Not at all

70. Worrying thoughts go through my mind.

A great deal of the time / A lot of the time / From time to time, but not too often / Only occasionally

71. I feel cheerful

Not at all / Not often / Sometimes / Most of the time

72. I can sit at ease and feel relaxed

Definitely / Usually / Not often / Not at all



73. I feel as if I am slowed down  
 Nearly all the time / Very often / Sometimes / Not at all  
 74. I get a sort of frightened feeling like 'butterflies' in the stomach.  
 Not at all / Occasionally / Quite often / Very often  
 75. I have lost interest in my appearance.  
 Definitely / I do not take as much care as I should / I may not take quite as much care as I ever  
 76. I feel restless as if I have to be on the move.  
 Very much indeed / Quite a lot / Not very much / Not at all  
 77. I look forward with enjoyment to things.  
 As much as I ever did / Less than I used to / Definitely less than I used to / Hardly at all  
 78. I get sudden feelings of panic.  
 Very often indeed / Quite often / Not very often / Not at all  
 79. I can enjoy a good book or radio or TV programme.  
 Often / Sometimes / Not often / Very seldom

80-85. We would like to know if any of the factors below have been affecting you over the last two months. If yes, please indicate how stressful these events have been for you. (If you would prefer not to answer, just click 'Next').  
 No / Yes - but not very stressful / Yes - moderately stressful / Yes - very stressful

New baby  
 Serious health problem affecting you, or someone close to you  
 Relationship problems  
 On-going financial strain  
 Bereavement of someone close to you  
 Any other recent event which you think has affected you?

86. Finally, the trial will involve listening to a 10 minute podcast every day. We'd like you to try and do this as frequently as you can over the next 2 months.  
 How confident are you that you will be able to set aside 10 minutes to meditate every day?  
 Not at all confident (1) \_\_\_\_\_ (5) Very confident  
 87. How confident are you that listening to the mindfulness meditation programme will change the way you feel about work?  
 Not at all confident (1) \_\_\_\_\_ (5) Very confident

Thanks. However confident you feel about whether the app will make a difference, the only thing we ask is that you give it a go with an open mind. When you miss a day, you can just pick up where you left off on the following day.

Brilliant! Thank you for completing the baseline survey.  
 If you have any questions, please ask the researcher or get in touch with the research team by email: [wellbeingapp@gmail.com](mailto:wellbeingapp@gmail.com)

## 8-Week Follow-up Questionnaire

As for the baseline questionnaire, plus extra questions for the first app group:

a) Which group were you allocated to in the trial?  
 \_First app group - you had instructions to download the app in September  
 \_Second app group - you haven't received any download instructions yet

b) Did you attend the launch event with Andy on the 10th September?  
 \_Yes  
 \_No

c) How would you describe your experience of the Headspace app?  
 \_I didn't download the app (owing to technical or other reasons)  
 \_I listened to a few days, but stopped after that  
 \_I meditated regularly at the beginning, but tailed off or had long gaps in my practice  
 \_I meditated quite regularly, between 2 and 4 days a week (on average)  
 \_I meditated routinely, 5 or more days per week (on average)

d) Do you think the time you have spent using the Headspace app over the last 8 weeks has made any difference to the way you think or feel now?

Please type in a few words or sentences about any changes you've noticed, positive or negative  
 \_\_\_\_\_ (type in)

e) Do you intend to continue meditating using the Headspace app over the next 8 weeks?  
 \_Yes  
 \_No

Please type in a few words to explain your answer

\_\_\_\_\_ (type in)

f) If you had a friend who was feeling stressed, would you recommend that they tried the Headspace app?  
 \_Yes  
 \_No

g) Finally, we'd like to improve the experience for Headspace users. We'd be really grateful for your suggestions. For example, these might be to do with the download or login process, audio or video content, reminders, design, the website - anything which occurs to you.

If I could change anything about Headspace, I would change.

\_\_\_\_\_ (type in)

WA \_\_\_\_\_

## HAIR Questionnaire

*Please only tick one box per question asked*

<b>a</b>	What is your natural hair colour?			
	All shades of...	Grey	Brown	
		White	Black	
		Blond	Other (please specify)	
		Red		

### DYE

<b>2</b>	Is your hair dyed?	Yes	No	→ Go to question 6
----------	--------------------	-----	----	--------------------

<b>3</b>	When did you last have it dyed?			
	Today	3-4 weeks ago		
	Yesterday	Over a month ago		
	A few days ago	Don't know		
	1-2 weeks ago			

<b>4</b>	What type of dye did you use?	Permanent	Semi-permanent	Don't know
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### PERM

<b>6</b>	Has your hair been chemically treated (eg. perm, chemical straightening)?			
	Yes	No	→ Go to question 9	

## 8.ix) Trial hair questionnaire

<b>7</b>	If you had any kind of chemical treatment, when did you have it done?			
	Today	3-4 weeks ago		
	Yesterday	Over a month ago		
	A few days ago	Don't know		
	1-2 weeks ago			

### WASH

<b>9</b>	How many times do you wash your hair <i>with</i> shampoo?			
	Daily	Once a week		
	4-6 times per week	Less than once a week		
	3-4 times per week (every other day)	Never		
	2-3 times per week	Don't know		

<b>10</b>	When did you last wash your hair with shampoo?			
	Today	3-4 weeks ago		
	Yesterday	Over a month ago		
	A few days ago	Don't know		
	1-2 weeks ago			

Late evening, before bed 22:00-23:00

ACTUAL TIME

22:08

22:08

**BP measure 1**

Systolic  mmHg

Diastolic  mmHg

Heart Rate  mmHg

**BP measure 2**

Systolic  mmHg

Diastolic  mmHg

Heart Rate  mmHg

Please tick the circle which best indicates how you're feeling now:

	Don't feel this way at all					Feeling is extremely strong				
Happy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>					
Angry or irritated	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>					
Sad or upset	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>					
Relaxed	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>					
Interested or engaged	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>					
Anxious or worried	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>					

**Feedback?**

Please make a note of any problems you had or anything unusual that happened during the monitoring.

Thank you very much for taking part. Please return your blood pressure monitor as soon as possible.



**Monitoring Diary**

**Well-being App Trial**

Start Date:

BP monitor:

Study ID:

- Please try to avoid eating, bathing, smoking and sport for 15 min before measuring your blood pressure.
- Sit on a chair with your feet flat on the ground and relax. Roll up your sleeve and remove your watch and/or bracelet to make sure the blood flow is not constricted.
- Fix the strap snugly around your wrist. Position your wrist at the height of your heart and support your elbow with other hand. Try and keep your back straight and your wrist relaxed.
- Press START, then keep your arm still. Don't speak during the measurement. Repeat after 2-3 minutes. Record the readings and your mood in this booklet.
- Please return the monitor to the research team as soon as possible after the last reading.

**Any questions?**

If you have any problems, please call Sophie Bostock 07779 578733 or email [wellbeingapp@gmail.com](mailto:wellbeingapp@gmail.com)

**8.x) Blood pressure and affect logbook**



Morning at home, before breakfast 06:30-08:30 ACTUAL TIME 7:27

BP measure 1

Systolic 118 mmHg

Diastolic 72 mmHg

Heart Rate 64 mmHg

Please tick the circle which best indicates how you're feeling now:

Don't feel this way at all Feeling is extremely strong

Happy 1 2 3 4 5

Angry or irritated 1 2 3 4 5

Sad or upset 1 2 3 4 5

Relaxed 1 2 3 4 5

Interested or engaged 1 2 3 4 5

Anxious or worried 1 2 3 4 5

BP measure 2

Systolic 110 mmHg

Diastolic 74 mmHg

Heart Rate 59 mmHg

Afternoon at work 16:00-17:00 ACTUAL TIME 16:14

BP measure 1

Systolic 123 mmHg

Diastolic 77 mmHg

Heart Rate 66 mmHg

Please tick the circle which best indicates how you're feeling now:

Don't feel this way at all Feeling is extremely strong

Happy 1 2 3 4 5

Angry or irritated 1 2 3 4 5

Sad or upset 1 2 3 4 5

Relaxed 1 2 3 4 5

Interested or engaged 1 2 3 4 5

Anxious or worried 1 2 3 4 5

BP measure 2

Systolic 119 mmHg

Diastolic 74 mmHg

Heart Rate 62 mmHg

Morning at work, before lunch 11:00-12:00 ACTUAL TIME 10:56

BP measure 1

Systolic 123 mmHg

Diastolic 82 mmHg

Heart Rate 58 mmHg

Please tick the circle which best indicates how you're feeling now:

Don't feel this way at all Feeling is extremely strong

Happy 1 2 3 4 5

Angry or irritated 1 2 3 4 5

Sad or upset 1 2 3 4 5

Relaxed 1 2 3 4 5

Interested or engaged 1 2 3 4 5

Anxious or worried 1 2 3 4 5

BP measure 2

Systolic 131 mmHg

Diastolic 84 mmHg

Heart Rate 65 mmHg

Evening 19:00-20:00 ACTUAL TIME 20:12

BP measure 1

Systolic 115 mmHg 121

Diastolic 69 mmHg 71

Heart Rate 72 mmHg 57

Please tick the circle which best indicates how you're feeling now:

Don't feel this way at all Feeling is extremely strong

Happy 1 2 3 4 5

Angry or irritated 1 2 3 4 5

Sad or upset 1 2 3 4 5

Relaxed 1 2 3 4 5

Interested or engaged 1 2 3 4 5

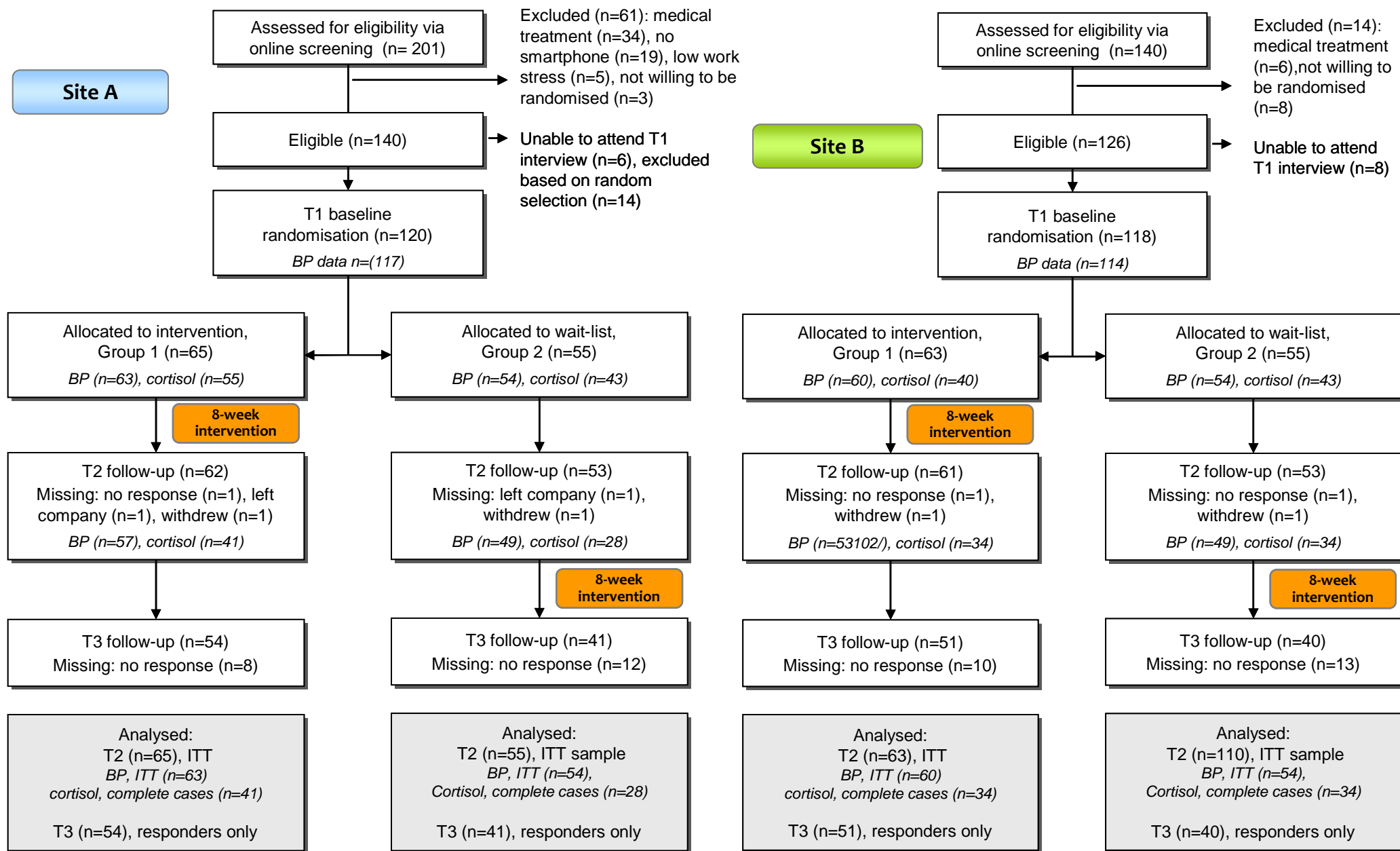
Anxious or worried 1 2 3 4 5

BP measure 2

Systolic 115 mmHg

Diastolic 71 mmHg

Heart Rate 54 mmHg



8.xi) CONSORT flow diagram for each site (Figure I)

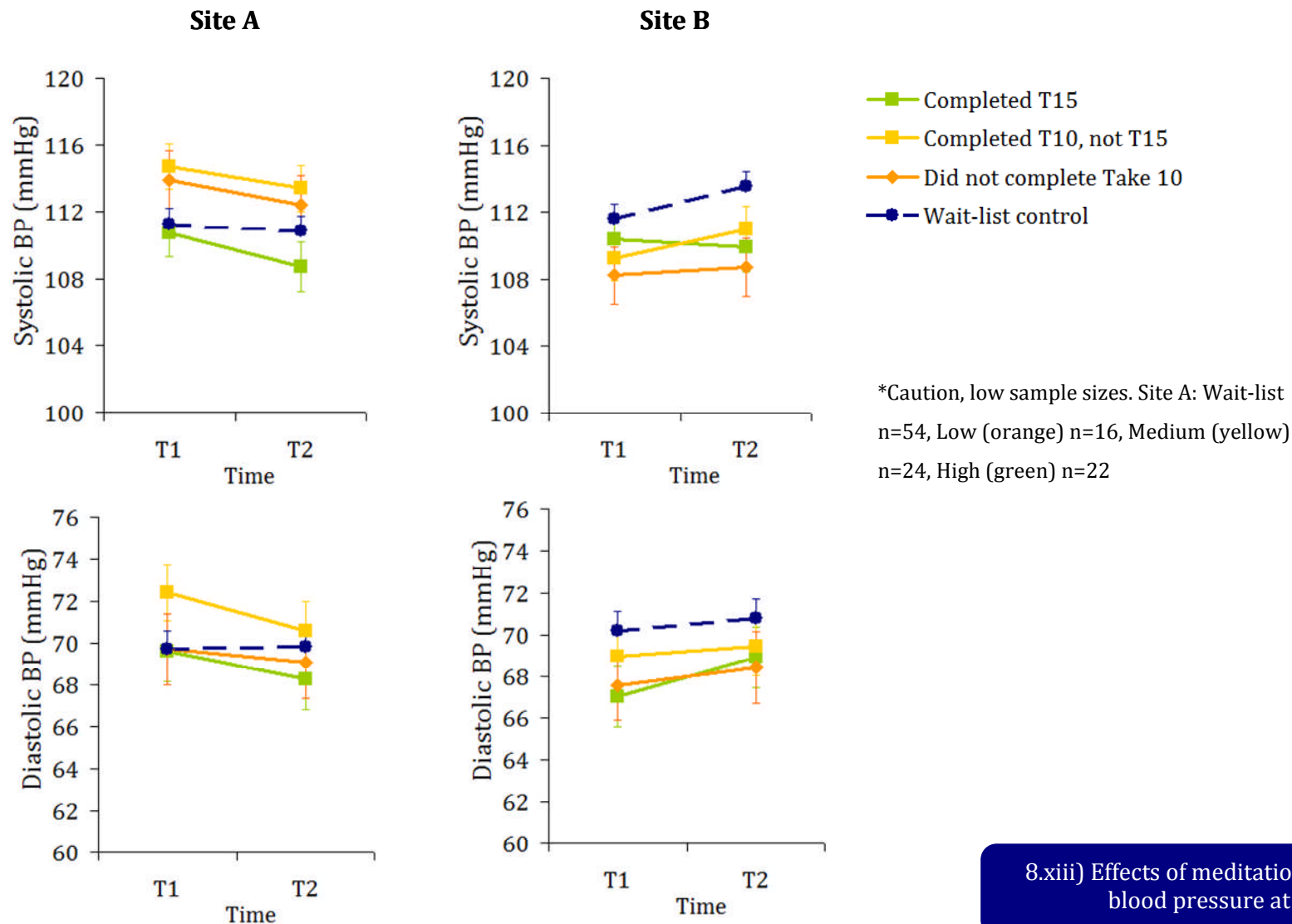
## 8.xii) Effects of allocation to app vs. wait-list group at each

**Table I** Repeated measures ANCOVAs, group (app/wait-list) by time (T1/T2) interactions and change scores (T2-T1) within each site

Outcomes	Site A				Site B			
	F (1,118)	$\eta_p^2$	Change scores, T2-T1		F (1,116)	$\eta_p^2$	Change scores, T2-T1	
			App group (n=65)	Wait-list group (n=55)			App group (n=63)	Wait-list group (n=55)
Well-being, WEMWBS	<b>4.03*</b>	0.37	<b>2.7 (5.7)^</b>	0.53 (5.9)	<b>4.82*</b>	0.41	<b>1.8 (5.6)^</b>	-0.40 (5.4)
Positive affect <sup>a</sup>	2.15	0.28	0.19 (0.48)	0.04 (0.60)	2.78	0.52	<b>0.10 (0.42)^^</b>	-0.12 (0.42)
Job strain	1.85	0.25	-0.06 (0.17)	-0.02 (0.18)	3.74	0.36	-0.03 (0.16)	0.03 (0.18)
Demands	0.012	0.02	-1.6 (10.4)	-1.8 (12.3)	3.08	0.32	-0.70 (9.4)	2.4 (9.7)
Control	<b>6.49*</b>	0.47	<b>2.9 (7.0)^</b>	-0.11 (5.2)	0.703	0.15	1.5 (5.5)	0.57 (6.8)
Social support	2.40	0.18	0.11 (0.50)	-0.03 (0.43)	2.24	0.28	0.14 (0.54)	0.01 (0.40)
Depression, HADS	<b>11.3**</b>	0.62	-1.8 (3.0)	<b>0.0 (3.0)^^</b>	<b>4.94*</b>	0.41	<b>-0.87 (2.7)^</b>	0.25 (2.8)
Anxiety, HADS	<b>4.16*</b>	0.37	-2.1 (3.7)	<b>-0.80 (3.2)^</b>	<b>4.00*</b>	0.37	<b>-1.2 (2.7)^</b>	-0.15 (2.9)
Negative affect <sup>a</sup>	<b>12.5**</b>	0.28	-0.19 (0.66)	<b>0.20 (0.55)^^</b>	0.062	0.09	0.09 (0.40) <sup>\$</sup>	0.05 (0.59)
Sleep problems	0.80	0.16	-0.28 (1.3)	-0.11 (0.79)	<b>6.00*</b>	0.45	-0.37 (0.75)	<b>-0.01 (0.84)^</b>
Mindfulness, FMI	<b>5.21*</b>	0.42	<b>2.9 (6.2)^</b>	0.5 (5.2)	<b>6.48*</b>	0.47	<b>3.4 (5.7)^</b>	0.98 (4.5)
Systolic BP, mmHg <sup>a</sup>	2.35	0.31	-1.6 (4.7)	-0.36 (3.2)	1.83	0.23	0.91 (4.0) <sup>\$</sup>	1.9 (4.5)
Diastolic BP, mmHg <sup>a</sup>	<b>6.84*</b>	0.41	-1.2 (3.3)	<b>0.03 (2.7)^</b>	0.13	0.09	0.87 (3.3) <sup>\$</sup>	0.59 (3.2)
Cortisol, pg/mg log <sup>b</sup>	0.119	0.002	-0.14 (0.39)	-0.12 (0.44)	0.068	0.001	-0.13 (0.38)	-0.14 (0.41)

<sup>a</sup> n=117 (A), 114 (B) <sup>b</sup> n=69,68, \*\*p<0.01, \*p<0.05. t-test, app group vs wait-list group ^^p<0.01, ^p<0.05. \$t-test app group at Site A vs Site B, p<0.05  
Combined site ANOVAs adjusted for site and change in work hours. BP analyses additionally adjusted for age, sex and bmi. Cortisol adjusted for hair dye and washing frequency.

**Figure II** Changes in systolic and diastolic blood pressure from T1 to T2 in wait-list (blue), low (orange), medium (yellow) and high (green) practice groups within each site



8.xiii) Effects of meditation practice time on blood pressure at each site\*

*Outcomes at T3, 8 weeks after the wait-list group accessed the app*

Between T2 and T3, the first app group reported a small uplift in anxiety,  $0.62 \pm 3.1$ , but all other psychological outcomes remained stable (Table). Forty-nine respondents (47%) claimed to have re-used the app since T2 but download data indicated that only  $n=28$  (27%) accessed new days of the programme (range 1-26 days, mean  $4.6 \pm 3.2$  days). Anxiety did not increase for those who listened to new days (mean difference  $-0.56 \pm 1.6$  for practice vs.  $0.73 \pm 3.2$  no practice).

The wait-list group completed  $13.6 \pm 11.2$  meditation sessions (range 0-45). T3 survey respondents reported significant increases in mindfulness and well-being, and reduced demands, job strain, anxiety and depressive symptoms. Changes in well-being and job strain for wait-list respondents from T2 to T3 were similar in magnitude to app respondents from T1 to T2. For example, for participants completing all surveys, increases in well-being post-intervention were  $+2.2 \pm 5.6$  for the app group  $+2.6 \pm 6.8$  for the wait-list group. There were no significant differences by site.

**Table II**      **Psychological outcomes assessed at T3 by experimental group**

	App group (intervention +10 wk)			Wait-list group (post-intervention)		
	T3 n=105	Change score T3-T2	t-test T3 vs. T2	T3 n=81	Change score T3-T2	t-test T3 vs. T2
Well-being (WEMWBS)	50.7 (6.6)	0.55 (5.5)	1.03	48.8 (7.5)	2.6 (6.8)	3.44**
Job strain	1.0 (0.2)	0.00 (0.2)	0.15	0.99 (0.2)	-0.06 (0.21)	-2.65*
Demands	81.3 (11.8)	0.24 (9.8)	0.25	76.5 (13.1)	-3.6 (13.1)	-2.45*
Control	78.9 (8.8)	-0.08 (5.8)	-0.14	78.0 (10.0)	0.55 (6.5)	0.75
Depression (HADS)	3.3 (3.1)	-0.10 (2.5)	-0.39	4.3 (3.5)	-1.1 (3.0)	-3.35**
Anxiety (HADS)	7.9 (3.6)	0.62 (3.1)	2.05*	7.9 (3.6)	-1.0 (3.5)	-2.65*
Mindfulness (FMI)	37.2 (7.0)	0.25 (4.6)	0.54	36.4 (6.2)	1.6 (5.5)	2.71**

\* $p < 0.05$ , \*\* $p < 0.01$ . Mean values (standard deviations in parentheses) at t3 based on complete cases. t statistic refers to paired t-test comparisons



*Open feedback about the experience of using the app*

The intervention group were asked an optional open question at T2 about whether using the app had made any difference to the way that they felt (Table). Across both sites, more than two thirds of those that responded mentioned positive experiences. Users were most likely to mention feeling more relaxed, but most did not specify whether this was directly after using the app or in daily life. Other users spontaneously mentioned benefits associated with mindfulness: becoming more aware of and less reactive to one's emotions and an increasing awareness of bodily sensations. Improved ability to cope with stressful situations and feeling more positive were also mentioned spontaneously. Those who didn't notice any changes typically blamed a lack of practice "not really, but that's more my fault than the app's; I just didn't have the time or mental energy to embark on it in this period". A minority of participants mentioned feeling worse as a result of participating in the trial, but for several this was owing to not finding time to meditate, "just feel a bit guilty for not having really got into it". One person mentioned finding becoming more physically aware an unpleasant sensation and another mentioned feeling emotional or vulnerable.

**Table III      Qualitative feedback about the effects of using the app**

*Q: Do you think the time you have spent using the Headspace app over the last 8 weeks has made any difference to the way you think or feel now? (free text)*

Spontaneous mentions			
	(n)		(n)
<b>Yes/positive response (any mention)</b>	<b>75</b>	<b>No difference (any mention)</b>	<b>21</b>
Feel calmer/more relaxed	35	Didn't meditate long enough/often enough	15
Enjoy using	17	Already practicing meditation/yoga	2
More aware and/or less reactive to emotions	18	Already felt positive	1
Notice breathing/physical awareness	11		0
Able to deal with stressful events	9		0
Feel more positive	7	<b>Negative effects (any mention)</b>	<b>8</b>
Appreciate taking 'time out'	6	Felt guilty/bad for not doing it	4
More alert/focussed at work	5	Came to resent 20 minutes for meditation	1
Improved sleep	6	Felt emotional/vulnerable	1
Less anxiety/worry	5	Felt more conscious of body (negative)	1
Improved social relationships	4	App was irritating	1
More patient/tolerant	3		